The British Veterinary Journal

JUNE, 1959

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Vol. 115 **June, 1959** **No. 6**

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EDITORIAL

BIG BUSINESS AND THE LAND

Basically, the good earth is the most important asset of the peoples of the world, for all terrestial living things depend upon it for their sustenance. It is true that there are other sources of food, such as the rivers and the sea, but their products, although delectable and nutritious, provide, at the moment, only a modicum of the essential requirements of life. They are as pepper and salt, and no one can live on condiments alone. For many centuries all men lived very close to the land and the prosperity of nations and the good health of the people could be measured according to the fertility of the soil. During the industrial boom of the Nineteenth Century when the mundane urge for monetary gain became the all-pervading motif of life many people turned their faces to the towns. They deserted the countryside to live in human warrens which soon became slums. Many of the migrants did not attain peace of mind, and deep in their hearts they yearned for the land and to till some of their own. This deep urge burns in many breasts today. The splendid cottage gardens, and even the window boxes in dull back streets, are a token of this desire. In most cases financial considerations debar any ambition greater than the joy of a small back garden but there has always been a return migration of those who, through the success of their economic adventures in commerce, are able to indulge their craving. The successful prodigals who respond to the call of the land have seen the world, have been in the van of progress and change, and have profited thereby. They know that the old ways, which had served so well in the past but will not suit the modern mode or pocket, must be changed.

Agricultural practice must be orientated so that it can conform to modern needs and economic standards. It is not sufficient to be a good husbandman in order to be a successful farmer. One must also acquire the attributes of a good economist and put them into practice. Good economy can be practised in any business, only, if sufficient capital is available to put schemes and programmes into action. The greatest foil to progress and complete success on the majority of farms is the lack of finance to take advantage of opportunities and expand, according to the demands of the time. Men with little professional knowledge of agriculture, but with capital at hand, can

farm successfully in places where others better versed in agronomy have failed to make a living. At the present time men with capital to spare, firms, institutions and other bodies, are investing in land. This is a sign of their faith in the future of agriculture. In consequence the value of land that was worth £25 an acre twenty years ago, has increased by several hundred per cent. Farmsteadings have been refurbished or replaced by others of modern design, thousands of pounds are spent on machines and the oil to run them and the quality and value of the stock has been enhanced far beyond previous comprehension. Big business has come to the land.

Is this a good thing and can it continue? There are those who have doubts. They point to the past in support of their arguments and in particular to the post Napoleonic and World War I periods. When the wars were in progress and times were dire agriculture was vital to the country's need and farmers prospered, but the flame of prosperity was snuffed at the peace table, and in the succeeding years the men of the countryside could fain make a living. One of the cogent reasons for the calamitous decline was, the capital, which had been fed liberally to agriculture in the emergency, was withdrawn and placed at more attractive financial advantage. There are signs that this calamity may not occur again. In our small islands first place must be given to the great financial and manufacturing industries if we are to survive as a first class nation. These things represent big business. With the development of mechanisation and the use of oil in agriculture big business has acquired a considerable financial stake in the land. If agriculture should return to the doldrums big business will be the loser and big business by keeping a sensitive eye and finger on world conditions loses but rarely.

OBSERVATIONS ON THE SEQUENTIAL APPEARANCE OF CENTRES OF OSSIFICATION IN THE DEVELOPMENT OF THE OSTEOCRANIUM OF OVIS (ORIENTALIS GMELIN)

by

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Introduction

A search of the literature reveals that no systematic study of the development of the asteocranium of Ovis has ever been attempted except by very few authors such as Claus (1911) and Lacoste (1927) who studied only the development of the interparietal and supra-occipitals. In the present investigation, an endeavour is made to trace the development of various bony constituents of the skull in Ovis, up to the stage studied by the author in the development of the chondrocranium (31 m.m. H.H.). Specimens of various sizes and ages have been subjected to mass staining by the Alizarin method to trace the ossified bones. The result obtained by this method has been confirmed by further study of the serial sections of embryos prepared for the investigation of the chondrocranium by the author. Eight stages of development have been dealt with under two headings, namely membrane bones and cartilage bones.

Material and Method

I have subjected the specimens mentioned below to the usual methods of mass staining by Alizarin Red S which do not require any detailed description.

Stage	I	13 m.m. H.H.
Stage	II	14 m.m. H.H.
Stage	III	16 m.m. H.H.
Stage	IV	17 m.m. H.H.
Stage	V	19 m.m. H.H.
Stage	VI	22 m.m. H.H.
Stage	VII	25 m.m. H.H.
Stage	VIII	31 m.m. H.H.

Serial sections, prepared for the study of the chondrocranium, have been used in correlating the results.

Observations

Stage I. 13 m.m. H.H.

Membrane Bones

The Dentary—This is the first membrane bone to develop and it attains considerable size. It extends along the Meckel's cartilage in an antero-posterior direction in the form of double lamellae, one on either side of the cartilage. The external lamella has attained a considerable length while the medial lamella is only a small

XUM

spicule projecting backwards from the anterior region. The anterior extremity is ill-defined and starts a little distance away from the symphysis of Meckel's cartilage. The dorsal and central borders are well defined.

The Frontal—This is a thin strip arching over the dorsal border of the orbit. Very few osteogenic fibres are seen at this stage.

The Maxilla—This is second in size when compared with the dentary. The main portion of the body is seen with the future infraorbital foramen in the form of a gap. Posteriorly it carries a thin blut process ventral to the orbit, the zygomatic process of the maxilla.

The Malar—This is a thin strip curving along the ventral surface of the orbit.

The Squamosal—This bone appears in the temporal region, dorsal to the auditory capsule. It is shaped like a club with the broad end posterior.

Cartilage Bones

As yet there is no sign of cartilage bone formation.

Stage II. 14 m.m. H.H. Fig. I.

Membrane Bones

The Dentary—There is not much variation in the size and length of the external lamella, whereas the medial lamella has extended further back reaching almost a third of the length of the mandible.

The Frontal—A slight increase in size is observed.

The Maxilla—The feature which draws attention in this region is the development of the palatine plate of the maxilla, which juts out medially like a shelf. No change in the size and shape of the bone is seen.

The Malar—There is no change from that of the previous stage.

The Squamosal—A slight increase in length anteriorly is perceptible. The bone shown a tendency to become flat posteriorly.

The Palatine—This bone appears for the first time at this stage. It is a thin streak situated at the posterior extremity of the palatine plate of the maxilla.

Cartilage Bones

Still no sign of cartilage bone formation.

Stage III. 16 m.m. H.H. Fig. II.

Membrane Bones

The Dentary—This bone has not only extended in length but also in height. The medial lamella has covered nearly three quarters of the length of the mandible. The coronoid process is seen extending backwards but there is no indication of the formation of the condyle. The mental foramen is like a longitudinal slit situated in the anterior region of the bone.

The Frontal—This shows considerable extension of ossification. The orbital plate comes into existence like a short strap descending downwards from the dorsal orbital rim. Besides the main body of the frontal bone another centre of ossification appears away from the main body and lying close to the mid-dorsal line.

The Parietal—This bone appears for the first time as a triangular piece posterior to the frontal. A wide gap intervenes between the centres on each side.

The Maxilla—This bone has increased in size. The infraorbital foramen, which was like a notch extending from the superior border of the bone, has closed and only the foramen for the passage of the infraorbital artery and nerve is left. There is a marked development of the palatine plate of the maxilla. It has extended backwards and is in confluence with the palatine bone. The zygomatic process has extended slightly in length beneath the malar and is like a blunt cone.

The Palatine—Both the horizontal and the vertical plates are visible.

The Premavilla—This bone appears for the first time like a thin streak anterior to the maxilla and represents the nasal process.

The Malar—This bone has developed further but remains unattached to the surrounding bones. It forms the ventral margin of the orbital cavity.

The Lachrymal—The lachrymal appears for the first time at the antero-internal angle of the orbit, like a small cone with the apex towards the malar.

The Squamosal—The zygomatic process stretches freely forward and the posterior portion has increased in size.

Cartilage Bones

The Hyoid—Reichert's cartilage has ossified at the posterior extremity near the auditory capsule.

This stage may be considered as one of the important stages, since many new centres of ossification have appeared; the parietal, the premaxilla, the lachrymal and the hyoid.

Stage IV. 17 m.m. H.H. Fig. III.

Membrane Bones

The Dentary—There is much change in the size and shape of this bone. The only feature which draws attention is the growth of the coronoid process which has become a big hook like structure extending backwards. The anterior and posterior borders are still ill defined. The mandibular symphysis is yet to be formed.

The Frontal—The two centres of ossification mentioned in the previous stage have coalesced, resulting in a broad plate like structure covering the major portion of the future cranium and extending from the posterior part of the nasal capsule to the parietal bone.

The Parietal—The area of ossification has increased slightly but a wide space still exists between the two bones.

The Maxilla—No perceptible change has taken place in this bone, except for the slight increase in length of the zygomatic process.

The Premaxilla—The nasal process has increased in size. The body and the palatine process have not yet appeared.

The Palatine—No change is visible from the previous stage.

The Pterygoid—This bone has appeared for the first time and only the hamulus is ossified.

The Malar—There has been slight increase in size.

The Squamosal—There has been an increase in the size of the body which has become like a curved plate.

XUM

Cartilage Bones

The Exoccipital—only the condyle portion has ossified.

The Hypoid—The part of the Reichert's cartilage described in the previous stage has developed further, into a well defined, deeply stained structure.

The new centres of ossification in this stage are in the exoccipital and the hamulus of the pterygoid.

Stage V. 19 m.m. H.H. Fig. IV.

Membrane Bones

The Dentary—The condyles are beginning to form.

The Frontal—The area of ossification has extended further and a distinct margin between the frontal and the orbital plate of the frontal, forming the dorsal margin of the orbital rim, is observed. The posterior border is still separated from the parietal.

The Parietal—The postero-external angle of this bone extends to meet the squamosal plate.

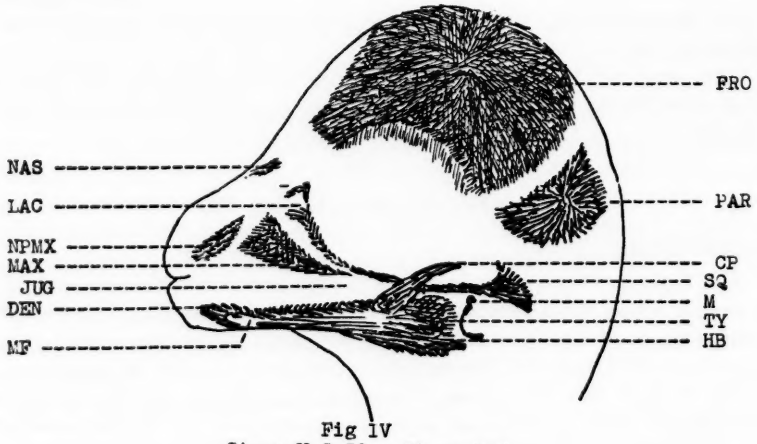

Fig IV
Stage V G 30 - 19 mm. H. H.

The Maxilla—The zygomatic process stretches further backwards and lies ventral to the malar. The alveolar border is observed as a wide gap between the body of the maxilla and the palatine process.

The Premaxilla—This bone is unchanged from the previous stage.

The Palatine—Both the horizontal and vertical plates are better ossified, their outlines are clear.

The Pterygoid—A rapid advancement over the previous stage is evident. The main body of the bone as well as the hamulus process is ossified.

The Malar—Posteriorly two processes are seen one above the other. The lower one is the longest. It extends below the zygomatic process of the squamosal.

The Lachrymal—In the previous stages only the facial part of this bone was recognisable but now the orbital part can be observed. It is pierced by a foramen, through which the nasolachrymal duct passes.

The Squamosal—There is a slight increase in the size of the body.

The Nasal—This bone appears over the roof of the nasal capsule, like a small island.

The Tympanic—The tympanic is like a thin strip, bent in the form of a half crescent, in the ventral portion of the auditory capsule.

The Vomer—This is represented by a thin streak of bone. It lies dorsal to the palatine plate of the maxilla, along the medial line of the skull.

Cartilage Bones

The Exoccipital—The extent of ossification of the condyle is the same as in the previous stage.

The Basioccipital—This bone arises as a median piece in the posterior portion of the basal plate. It has the appearance of an oval plate.

The Basipostsphenoid—Arises in the hypophyseal cartilage. It resembles a short oval rod placed transversely to the congitudinal axis of the skull.

The Alisphenoid (wing of the postsphenoid)—This is formed by the ossification of the alar process and the ala temporalis. It is like a fork with a handle.

The Orbito-sphenoid (wing of the presphenoid)—Arises in the ala orbitalis, lateral to the optic nerve. The ossification extends like a crescent from the pre-optic root of the ala orbitalis. The body of the presphenoid has not ossified.

The Hyoid—There is no change over the previous stage.

The Malleus—The ossification centre appears in the neck of the Meckel's cartilage like a small triangle.

It is interesting to note that several new centres of ossification have appeared in the chondrocranium between stage IV and stage V. The new centres in stage V are the mandibular condyle, the tympanic, the vomer, the basioccipital, the basipost-sphenoid, the alisphenoid, the orbito-sphenoid, the nasal, and the malleus.

Stage VI. 22 m.m. H.H. Fig. V.

Membrane Bones

The Dentary—The medial and lateral lamellae have reached the full length of their growth. The condyle is still developing. The alveolar border is identified as a raised ridge on the dorsal border of the horizontal part of the mandible.

The Frontal—No development beyond the previous stage is noted.

The Parietal—The ossification has spread over a greater area, resulting in a narrowing of the gap between the two bones.

The Nasal—There is slight increase in the size of the bone.

The Maxilla—There is no change, except for a slight increase in size.

The Premaxilla—The body and the palatine process have appeared by this stage. The nasal process has extended a little further backwards and is in contact with the anterior border of the body of the maxilla.

The Palatine

The Pterygoid—These bones show no advance on the previous stage.

The Malar

The Lachrymal

The Squamosal—The body has expanded and the zygomatic process has a twisted appearance.

The Tympanic—There is a marked increase in the length of the bone and it is semicircular in appearance.

The Vomer—The ossification has extended in an antero-posterior direction, resulting in the formation of a long scroll-like bone.

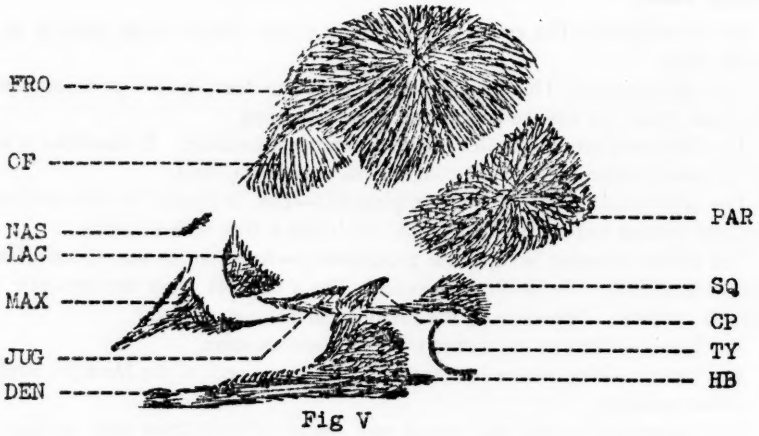

Fig V

Stage VI G 3 - 22 mm. H. H

Cartilage Bones

The Exoccipital—The condyle is more prominent than in the previous stage and its root is surrounded by a greater area of ossification.

The Basioccipital—A slight increase in size is noted.

The Basipostsphenoid—This has increased in length and width.

The Alisphenoid—The ossification has spread medially and the bone has met the basipostsphenoid which has extended laterally. There is no change in the size and shape of the fork-like wing of the postsphenoid.

The Orbitosphenoid—Both the pre-optic and the met-optic roots of the ala orbitalis are ossified, giving the final shape to the optic foramen. The latter looks to be complete except at the medial boundary. The body of the presphenoid which is not yet ossified.

The Hyoid—There is no change in the area of ossification.

The malleus—The bone is more defined and there is slight increase in the area of ossification.

Stage VII. 25 m.m. H.H. Fig. VI.

Since there is not much change in many of the bones, only new centres of ossification are mentioned.

PLATE I

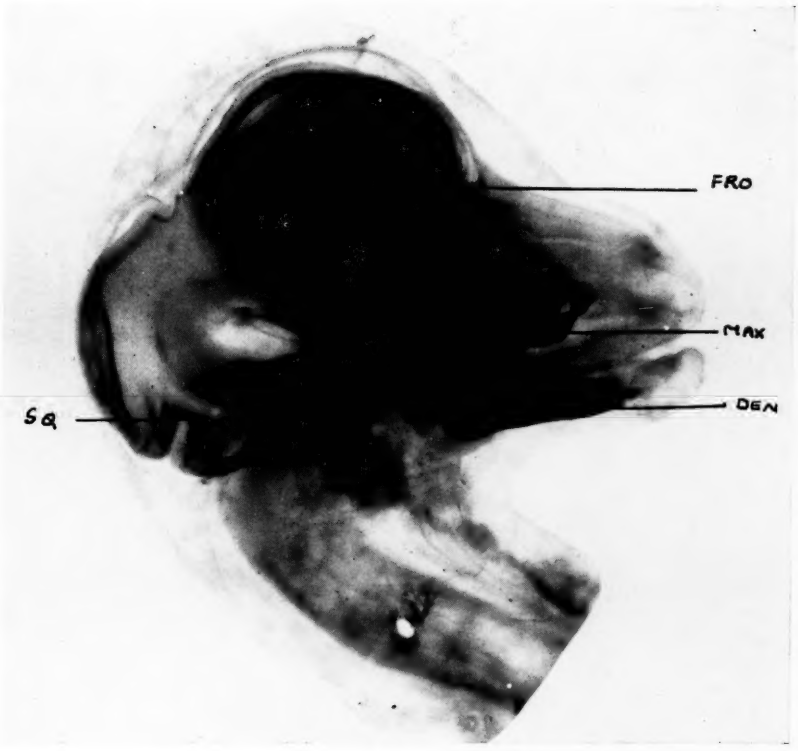

FIG. I

Stage II G 33-14 m.m. H.H.

ALI—Alisphenoid bone
BO—Basioccipital bone
CP—Coronoid process
DEN—Dentary bone
FRO—Frontal bone
HB—Hyoid bone
JUG—Jugal bone
LAC—Lachrymal bone
M—Malleus
MAX—Maxillary bone
MF—Mental foramen
MF—Foramen mentale
NAS—Nasal bone
NPMX—Nasal process of Pre-Maxillary bone
OC—Occipital condyle
OF—Orbital plate of Frontal bone
ORS—Orbitosphenoid
PAR—Parietal bone
SOB—Supraoccipital bone
SQ—Squamosal bone
TY—Tympanic bone

(*Article by C. V. Kanan on pages* 185-194)

PLATE II

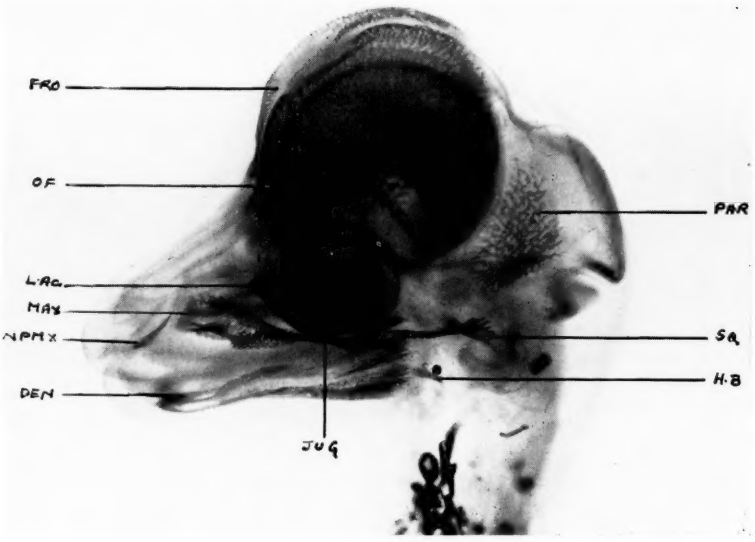

FIG. II
Stage III G 4-16 m.m. H.H.

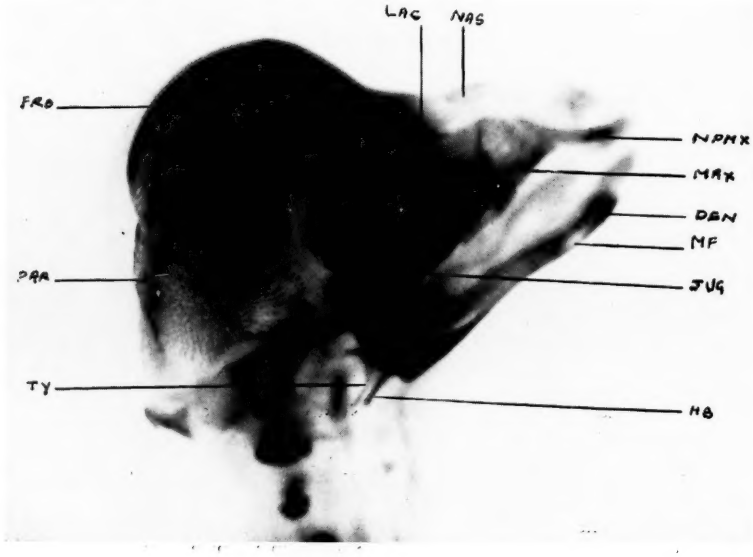

FIG. III
Stage IV G 34-17 m.m. H.H.

(*Article by C. V. Kanan on pages* 185-194)

Membrane Bones

The Interparietal—This bone appears as an irregular piece at the postero-internal angle of the parietal on each side. It is important to note that the interparietal has two centres of ossification one on either side of the medial line.

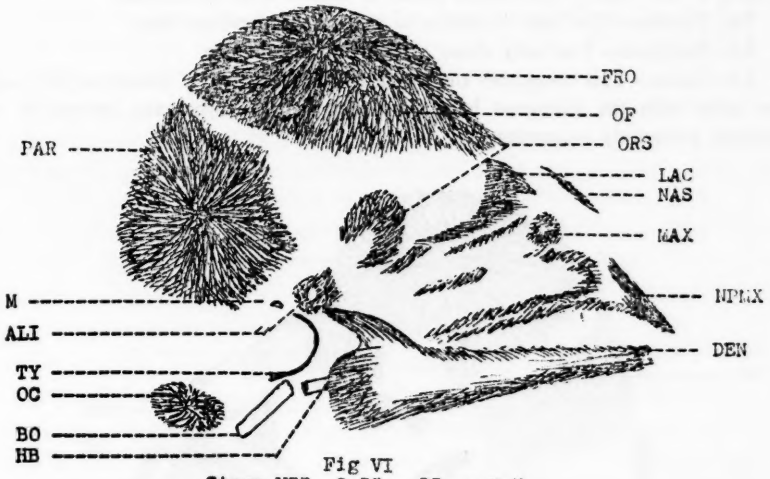

Fig VI
Stage VII G 35 - 25 mm. H. H

Cartilage Bones

The Occipital arch (supra occipital) appears in the region of the tectum posterius as a small triangular piece of bone in the mid dorsal site, with the base facing the interparietals and the apex towards the foramen magnum.

The Alisphenoid (wing of the postsphenoid)—The fork-like structure observed in the previous stage has ossified further completing the foramen ovale, through which the mandibular branch of the trigeminal passes.

Stage VIII. 31 m.m. H.H. Fig. VIII.

Membrane Bones

The Dentary—The mandibular symphysis is not yet formed so the dentary of one side is separated from its fellow on the opposite side by a narrow space. The various constituent parts of each half may now be recognised; the ramus, the angle, the coronoid process, and the condyle.

The Frontal—This bone has reached its full size and the orbital plate extends up to the orbitosphenoid bone.

The Nasal—There is increase in size and the bone appears as an oval body with the base towards the anterior border of the frontal bone.

The Parietal—With increase in the area of ossification, the space between the two bones has narrowed.

The Interparietal—There is no change from the previous stage.

The Maxilla—There is a general increase in size and the anterior border is in contact with the nasal process of the premaxilla. The zygomatic process is in contact with the ventral surface of the zygomatic arch the facial tuberosity can be recognised as a laterally producing mass with the infraorbital foramen at its anterior end.

The Premaxilla—The only noteworthy change at this stage, is the backward extension of the nasal process which comes in contact with the maxilla.

The Palatine—The bone is similar to that of the previous stage.

The Pterygoid—The body shows a slight increase in size.

The Malar—This completes the zygomatic arch, which is firmer at this stage, since union with the lachrymal bone anteriorly and the zygomatic process of the squamosal posteriorly is complete.

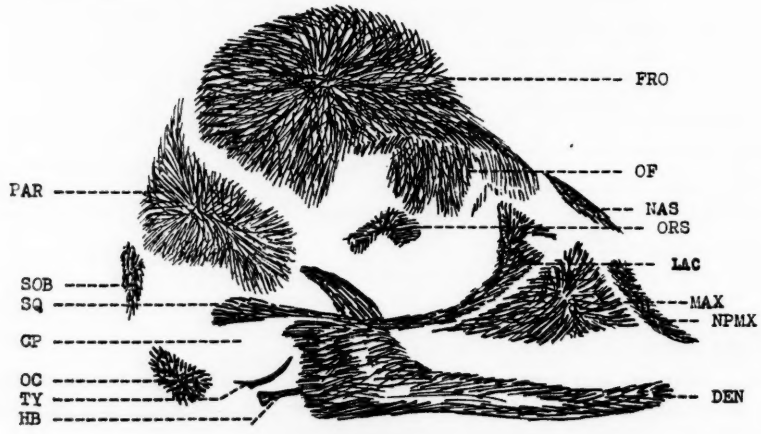

Fig VII
Stage VIII. G29 -31mm.H.H.

The Lachrymal—There is slight general increase in size.

The Squamosal—The zygomatic process presents a twisted appearance and ventrally it shows the formation of the condyle for articulation with the mandible.

The Tympanic—There is no change.

The Vomer—There is no change.

Cartilage Bones

The Exoccipital—There is no change.

The Basioccipital—The anterior portion has extended so that the bone has changed from an oval to a flask-like shape.

The occipital arch—Resembles two oval bodies, whose medial borders are continuous, and it has a cleft posteriorly.

The Basipostsphenoid—The breadth of this bone has increased, giving the appearance of a flat band running transversely.

The Alisphenoid

The Orbito-sphenoid—No change.

The Hyoid

The Malleus—The area of ossification has increased and the bone looks like a small triangle at the neck of the Meckel's cartilage.

The important changes, at this stage, are the formation of the angle and the condyle of the mandible and the extension of the orbital plate of the frontal.

Summary

1. Though the cartilages of the chondrocranium appear early in the development of an embryo, their ossification is preceded by that of some of the membrane bones.
2. The first membrane bone to appear is the dentary.
3. The frontal and the parietal bones develop more rapidly than any other bones of the cranium and so form an effective roof over the brain.
4. The interparietals have two centres of ossification and therefore there are two separate pieces of bone instead of a single piece in the middle.
5. The basisphenoid and the auditory capsule do not ossify till late in the development.
6. The malleus is the first to ossify amongst the auditory ossicles.
7. With the exception of a portion of the Reichert's cartilage no other part of the hyoid arch is ossified till late in the development.

Discussion

The earliest specimen to show the membrane bones, in a feebly developed state, is that of 13 m.m. H.H. The dentary is in a fairly advanced stage of development. Previous authors have established that the dentary is the first membrane bone to develop and this is confirmed in this investigation. The dentary is seen as a flat piece of bone extending along the Meckel's cartilage. The growth of this bone has been followed in this study and the following observations are noteworthy. The Meckel's cartilage takes no part in the formation of the mandible, it serves only as a supporting rod to the developing dentary. The dentary is composed of two lamellae, the medial and lateral, which develop at different rates. The medial lamella grows more slowly than the lateral and attains its full length in a specimen of 22 m.m. H.H. The mandibular symphysis does not occur till late in the development of the osteocranium. The development of the condyle of the mandible is preceeded by the coronoid process.

The frontal and the parietal bones develop rapidly in order to protect the brain.

The interparietals ossify from a paired centre posterior to the parietals. The preinterparietal centres found occasionally in Bos, Canis and Man were not seen in any specimens of Ovis.

Of the facial bones, the maxilla is the first to attain a considerable size. The nasal process (ascending process) of the premaxilla develops first and it takes some time for the body and the palatine process to develop. Gaupp (1906) and Schwink (1888) observed that the palatine process of the premaxilla in Ovis had a separate centre of ossification and became fused to the process directed backwards from the body of the premaxilla. In the present investigation the palatine process of the premaxilla was attached already to the body and at no stage did it exist as an independent structure. The body and the palatine process appeared together in the 2 m.m. H.H. specimen. It may be said that the palatine process of the premaxilla represents the prevomer of the earlier forms which has lost its individuality.

The first part of the Pterygoid bone to appear in Ovis is the hamular process in a 17 m.m. H.H. specimen followed by the internal pherygoid plate. In man, Fawcett (1905 and 1910 A and B) has described the internal pherygoid bone as ossifying earlier than the hamular process. Though the membranous part of the pterygoid bone is well formed, the pterygoid cartilage of the ala temporalis remains unossified for some time, showing that the pterygoid bone of the adult is a combined structure of two distinct pieces of bone derived from different origins, membranous and cartilaginous. This observation is in accordance with those of Broom (1914), Gaupp (1901), Juchs (1909), Kampen (1922), Terry (1917), Fawcett (1905), and Lubosch (1907) in regard to other mammals.

It is noteworthy that of the cartilage bones the Reichert's cartilage is the first to ossify, though it is formed much later than the other cartilages of the chondrocranium. This is followed by the occipitals. The alisphenoid (wing of the postsphenoid) ossifies earlier than the basipostsphenoid. It is in the shape of a fork with the processus alaris serving as a handle. Further ossification leads to formation of the foramen ovale. The mandibular branch of the trigeminal nerve passes through this foramen. Another fact which attracts attention is the absence of ossification of the basisphenoid, though the orbitosphenoid (wing of the presphenoid) ossifies simultaneously with that of the alisphenoid.

The supraoccipital (occipital arch) of Ovis ossifies from a median unpaired centre in the tectum posterius. This is in agreement with the observations of Lacoste (1927) in Ovis, Drews (1933) in Felis, Augier (1934) in Sus, where as in Bos, Augier (1931) and Canis, Drews (1933), it arises from paired centres.

The posterior extremity of the Meckel's cartilage is the first of the auditory ossicles to show signs of ossification. Though it is not intended to give a detailed description of the origin of these bones it may be said that the malleus, incus, and stapes of mammals are homologues with the articular, quadrate, and columella auris of reptiles.

It may be mentioned in conclusion that, though the chondrocranium develops as scaffolding material for the future building of the osteocranium, it is not till late in the development of the membrane bones that the ossification centres appear in the various cartilages of the chondrocranium.

REFERENCES

Augier, M. (1931b): *Arch. Anat. Strasbourg, 13,* 33.
Augier, M. (1934a): *Arch. Anat. Strasbourg, 19,* 89.
Broom, R. (1914): *Philos. Trans, B. 206,* I.
Claus, T. (1911): *Anat. Anz. 39,* 364.
de Beer, G. R. (1937): The Development of the Vertebrate Skull. Oxford.
Drews, M. (1933): *Morph. Jahrb., 83,* 185.
Fawcett, E. (1905c): *J. Anat. Lond., 39,* 439.
Fawcet, E. (1910a): *J. Anat. London., 44,* 207.
Gaupp, E. (1901): *Ergebn. Anat. Entwesch., 10,* 847.
Gaupp, E. (1906b): *Verh. anat. Ges. Jena., 20,* 21.
van Kampen, P. N. (1905): *Morph. Jahrb., 34,* 321.
Lacoste, A. (1927): *C. R. Soc. Biol., Paris, 97,* 1403.
Lubosch, W. (1907): *Denkschr. med-naturw. Ges. Jena., 7,* 519.
Parker, W. K. (1874): *Philos. Trans., 164,* 289.
Schwink, J. (1888): Uber den Zwischenkiefer und seine Nachbarorgane bei Säugetieren, München.
Terry, R. J. (1917): *J. Morph., 29,* 281.

DISPLACEMENT ACTIVITIES IN DOMESTIC ANIMALS

by

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History

Study of irrelevant behaviour particularly in fish and birds, mainly by Tinbergen, led to the wider recognition of a group of behaviourisms called displacement activities. Earlier zoological workers, e.g., Kirkman (1937), had become interested in the phenomena of these movements in lower animals and Tinbergen's observations supported, confirmed and enlarged upon the findings of other workers. A change in terminology was suggested. Bierens de Haan, one of the first of the many psychologists to become interested in the discovery, called them substitute reactions. This latter or "substitute behaviour" would be perhaps more apt terminology. However, Tinbergen in his later writings referred to them as displacement activities and this nomenclature is now in popular use (Lorenz 1953). This increased usage makes any alternative name unlikely to find general acceptance and, in fact, common use will make the name secure, although it appears clumsy at first.

Definition

In its descriptive role the term "displacement activities" is quite satisfactory. It suggests that the behaviourisms under study are specific activities which are displaced from their normal position and this is certainly the case. When observed, such displacement activities appear to be quite irrelevant (Rand, 1943), and indeed it is widely held that their irrelevant occurrence in behaviour is an essential feature of their identity. Recently, however, Andrew (1956a) points out that in *Emberiza sp.* certain behaviour patterns which are displacement activities are really caused to occur in the same way as in their normal functional occurrences and are only apparently irrelevant. This, however, scarcely affects the validity of the original conception. This irrelevance, or apparent irrelevance, provides the displaced character of displacement activities. The activities themselves are to be seen as innate behaviour patterns and this is invariably so. As a result, they are to be seen as forms of such instincts as fighting, eating, drinking, sleeping, grooming and sexual behaviour.

Identifying Features

The casual factor of displacement activities has been described as a "sparking over" of a drive, so that an instinct totally independent of that drive becomes motivated. For example, the domestic cock, when strongly aroused and engaged in fighting, may suddenly discontinue the fight and peck at the ground as though feeding. However, it appears that "sparking over" of a stimulus, as it was first referred to by Makkink (1936), depends on an excessive degree of stimulation occurring whilst at

the same time a normal response to that stimulation is hindered. As a result, surplus motivation becomes established in the animal and this finds outlet in some other activity. Fundamentally, then, the mechanism of displacement activities is this. An instinct becomes prompted, and eventually very strongly motivated, but the customary response in behaviour is blocked for some reason and the drive which is thus undischarged becomes applied to some instinctive behaviour which is not blocked at that moment so that an act is produced which is apparently unrelated to the original stimulus. So it is seen that common enough acts and movements can suddenly appear in behaviour, but because they are not the usual movements for the instinct which is activated at the instant of observation, they are seen to constitute unusual behaviour.

There is always physical evidence of strong motivation in the individual enacting a displacement activity. Such an animal is seen to appear highly nervous or excited. This is shown by general restlessness and by the vigour with which the animal usually performs the displaced act. Although vigour is often shown, it is seldom that the act itself is completely and properly executed. For example, whilst displacement chewing among cattle represents the instinct of feeding, it is usually unaccompanied by swallowing so that the elaborate chewing movements, although vigorous, fall short of the complete behaviour pattern which has been irrelevantly adopted. Nevertheless, it has been suggested that the greater the initial motivation, the greater is the likelihood of the displacement activity appearing in more complete form.

The factors creating the inhibition, that is, those commonly responsible for blocking the outlet of instinctive behaviour, have been studied. Tinbergen considers these factors with regard to the lower animals in two groups:—

(a) "Conflict of two strongly activated antagonistic drives"—commonly, fighting and fleeing;

(b) "Strong motivation of a drive, usually the sex drive, but at the same time lack of external stimuli required for the release of the consumatory acts belonging to that drive."

Haan mentions early arrival at a given goal, or premature achievement of purpose to be another causative factor. This is associated sometimes with copulation.

Casual Factors in Domesticated Species

A study of displacement activities in domestic animals shows the factors inhibiting behaviour release to be commonly in the following categories:—

1. Inhibition by fear. Fear is often seen as a deterrent to positive action, and a fear-like state in the animal is sometimes responsible for the prevention of the behaviour which has been stimulated. In such circumstances, the response of flight is antagonistic to the other response stimulated and this is a situation similar to that mentioned above in (a). In addition, the circumstances of domestication often cause the restriction of flight. A sow in an apparent state of fear, being newly farrowed and being attended by an over-anxious owner, was seen to avoid the piglets and indulge in prolonged spells of displacement chewing and rooting in a trough of dry meal during which little or no food was actually consumed. Here it was believed that the increased apprehension attendant on parturition prompted the perception of threat in the

appearance of the attendant and the resulting fear conflicted with the instinctive desire to suckle the new-born litter created a blockage to maternal behaviour and gave rise to a displacement activity.

2. Inhibition by conditioning. Repeated experience may establish an inhibition. For example, a young, immature bull was used excessively in a herd of cows and soon he refused to copulate on occasion. Increasing use led to more frequent refusals until all copulation was refused. Seen at this time, the bull, after considerable stimulation, indulged in displacement butting and goring on the cow. In this connection it may be said that conditioned inhibition of copulation resulting in unwillingness to consummate in the face of normal stimulation is a common circumstance producing displacement activities and thereby resembles (b) above.

3. Physical inability. An obvious reason why an animal may be unable to execute normal behaviour response is that when the subject is physically unable to do so as, for instance, from temporary physical exhaustion. A newly calved cow suffering from metritis and septic bursitis of both hocks was lying down for lengthy periods out of doors, unable to walk away from onlookers. She became 'excited' during an examination and began biting and tearing up pieces of turf and chewing them with vigour. Any supposition of a hearty appetite, however, would have been quite inaccurate.

It has been stated earlier that displacement activities appear in the form of instinctive patterns of behaviour, and many such examples have been shown to occur in birds, as fighting, eating, sleeping, grooming (that is, care of the body surface) and courtship—Tinbergen (1951) and Andrew (1956b). In the domestic animals, examples of displacement activities employing various instinctive movements have been observed.

Instincts Employed in Domesticated Species

Sleeping: The somnolent condition of the bull is recorded by Kerruish (1955) who acknowledges its earlier description by Russian workers. In this condition, the bull adopts a characteristic posture. Such a subject, after ejaculation, shows marked relaxation, and will stand behind the cow with the head on the latter's hind quarters and the eyes half closed. This state has been observed by the writer on a number of occasions and the appearance of sleep can sometimes be very real and sustained for lengthy periods. The condition closely resembles the displacement sleeping or resting attitude of yellow hammers after attempted copulation as described by Andrew (1956b). This somnolent condition in the bull is almost certainly a displacement activity involving the instinctive behaviour of sleeping. Kerruish further states that, in general, the condition is characterised by a lack of undivided concentration upon the sex act and gives another example of this diverted attention at copulation when the bull attempts horn play with the cow and avoids copulation. A similar type of event has also been described above and provides an example of yet another instinct employed in displacement actions, that is, fighting.

Fighting: Bulls which do not undertake copulatory attempts for various reasons, e.g., through a sexual inhibition, can sometimes be seen to indulge in goring or butting on the cow, and it is believed that this goring behaviour is a true displacement activity employing the fighting instinct. Parallel behaviourisms are recorded in birds.

Feeding: The feeding or eating instinct is, of course, commonly employed in displacement activities, and many examples are recorded in lower animals. In domestic animals cannibalism in the emotionally disturbed (strongly motivated) sow suggests itself as an example, but a more certain illustration of its occurrence is that mentioned earlier where a sow demonstrated both rooting and chewing movements in a displacement activity. No food was actually consumed, but this incompleteness of the act is a common feature of displacement activities, as has already been mentioned. Very earnest displacement chewing or biting has been observed by the writer on innumerable occasions in virtually all the domestic species including horses, cattle, sheep and dogs.
Grooming: It has been established that care of the body surface is a true instinct (Tinbergen 1951) and in cattle this instinctive grooming behaviour can appear as licking (Brownlee, 1951). Examples of such behaviour being used as displacement actions have been observed. It has been considered that in acetonaemia with anorexia suppressing feeding activity, excessive self grooming occurs and this might be a displacement activity. Certainly, displacement grooming by bulls does occur. This is to be seen after a bull has made a number of unsuccessful mounting attempts with a restless cow. In such circumstances he often engages in active licking on the part of the cow which is presented to him. The element of social significance in displacement activities, as described by Tinbergen, is suggested here since the cow is often observed to become less fractious after such grooming.
Sexual Behaviour: It is known that sexual movements in lower animals such as birds occur as outlets of the fighting instinct. In domestic animals, too, sexual behaviour is often utilised in displacement actions. One example will be sufficient to illustrate this point. Dogs of both sexes which are caused to become "over-excited" as, for example, from fondling, will often make copulatory actions on the persons of attendants. This action can become established as habit. Initially, this is a true displacement activity. The highly motivated animal finds an energy outlet in an irrelevant instinctive behaviour pattern.

General Considerations

The initial motivation seems to be satisfied by the substitution, but although it is seen that the phenomenon appears in differing behaviourisms, it is not suggested that they are adopted haphazardly. The displacement activity enacted is essentially one which the milieu permits at the moment of motivation. Other deciding factors may exist, but at present are unrecognized.

To conclude this consideration of some of the instincts which are employed in displacement acts, it may be of interest to note that in one selected subject alone, namely the bull, the writer has observed the use of all these instincts mentioned in executing a variety of displacement activities. The recognition of a displacement activity in the bull is also recorded by Schloeth (1958).

The constancy of recognizable displacement acts for given situations and species is remarkable. Illustrative of this is the somnolent conditions in bulls universally recognized, but perhaps unidentified, by cattle breeding workers but now shown as a displacement activity. Tinbergen also finds such stereotyped behaviour in lower animals remarkable and suggests a theory in which "the motivation of an instinct

when prevented from discharging through its own motor pattern, finds an outlet by discharging through the centre of another instinct". This theory is quite acceptable, but it does not fully explain the strict constancy of displaced behaviour. It would still allow variation in displacement activities for a given situation in a species from time to time, and this does not appear to happen.

It has been acknowledged above that the circumstances of domestication often inhibit escape responses. Indeed, where the animal is closely confined and supplied with all its food, the activity of food searching (a fundamental one) is completely prohibited. General activity is also restricted. These are common enough circumstances in domestication, and it is found that such confinement is often instrumental in the production of a type of displaced activity which can be considered as the domestic group of displaced acts. These actions may not always measure up to earlier classic examples with regard to clarity of defining features, but their importance is real. This importance does not lie in the academic field so much as in the sphere of veterinary clinical methods.

In the horse, crib-biting and wind-sucking (both representing fragments of feeding activity) could readily be considered displaced actions of the domestic group. Other examples of such activities which are associated with housed restriction include defecation by stall-tied cattle when alarmed as, for example, on the sudden appearance of a stranger. Coprophagia of housed foals could also be considered as behaviour coming within this category. The scratching of furnishings by indoor cats and excessive self-grooming by housed calves in good condition are other examples of this "domestic type" of displaced act.

These examples are not wholly speculative. Observations on them reveal a good many of the components known to be associated with the manifestation of displacement activities and, in fact, the greater plasticity in behaviour which is expected of the higher groups of mammals could be considered as the modifying factor in these actions. It is thought that wider observations may reveal a store of substitute behaviour of veterinary significance in the domestic species.

General Theory

Finally, not the least important aspect of displacement actions is the indication that their fundamental processes extend into more complex behaviour. We begin to conceive that displaced acts may be but one specific manifestation of a general psychological law which governs in many circumstances. For instance, it is popularly known that the captivity and isolation in a zoological park are often conducive to what we might term "zoo behaviour" — the monotonous repetition of movement. This can be seen in the swaying movement of polar bears and the figure of eight movement of wolves and other animals. Katz (1953), in discussing such behaviour, states: "if the natural urge for movement is frustrated, it tends to find an outlet in such stereotyped forms." Stereotyped acts in the form of "tics" are well-known even out-with the zoo. In spite of resemblances none of these acts could be accurately classed with the displacement activities demonstrated in lower species. Apart from tics, other behaviourisms are seen to occur irrationally in the individual under strong motivation. For instance, it is common knowledge that in the domesticated species

attacks on the new-born by the stimulated mother occur from time to time. These attacks are usually effected vigorously, and there is a striking similarity to our concept of displacement actions. However, the response is too elaborate and the exact stimulus difficult to define so that we cannot afford them exact classification. As with the domestic group of displacement acts mentioned above, these behaviourisms do not match exactly the displacement activity model. However, the fundamental mechanism appears to be similar throughout and there is mounting evidence of the need to appreciate a much wider concept of irrelevant behaviour.

Hypothesis

The existence of a fairly comprehensive law governing the automatic release of excess psychic energy in behaviour of a type which has, to some extent, been previously shaped whether innately or by learning now seems to be strongly suggested. The existence of a comprehensive law of this nature has previously been suggested, originally by Darwin, and later by a number of psychologists. The further recognition of the more plastic type of transferred behaviour by which displacement activities appear in domestic animals may establish further support for this theory. At the same time, the complexity of response shown in some of the examples mentioned above could be taken as supporting evidence for Barnett's theory in which he claims that a link exists between the displacement activities so thoroughly investigated at the experimental level by many ethologists and the psycho-somatic states known to occur in man.

Additional confirmation of such a link would go a very long way towards establishing a comprehensive law of substitute behaviour which has been roughly outlined here.

Summary

The history and existing knowledge of displacement activities is given in brief.

The occurrence of these actions in domesticated species of animals is shown.

The causal factors of displaced acts in such animals is discussed and the various instincts used in these acts is alo recorded.

The existence of modified forms of displaced acts in domestic animal behaviour is described.

The wider occurrence of substitute behaviour in various forms is mentioned.

A hypothetical theory governing the enactment of substitute behaviour in general is suggested.

REFERENCES

Andrew, R. J. (1956a): Some remarks on behaviour on conflict sits. with special reference to Emberiza. *Spp. Brit. J. Anim. Behav., 4,* 41-45.

Andrew, R. J. (1956b): Fear responces in Emberiza. *Spp. Ibid, 4,* 125-132.

Barnett, S. A. (1957): The Expression of the Emotions. *New Biol., 22,* 73-90.

Brownlee, A. (1951): Studies in the behaviour of domestic cattle. *Vet. Rec., vol. 63,* 443.

Darwin, C. (1872): The Expression of the Emotions in Man and Animals, London.

Haan, J. A. B. De. (1948): Animal Psychology. Hutchinson's University Library, London.

Katz, D. (1953): Animals and Men, London.

Kerruish, B. M. (1955): The effect of sexual stimulation prior to service on the behaviour and conception rate of bulls. *Brit. J. Anim. Behav., 3,* 125-130.

Kirkman, F. B. (1937): Bird Behavior London. Edinburgh.

Lorenz, K. (1953): King Solomon's Ring. Reprint Socy., London.

Makkink, G. F. (1936): An attempt at an ethogram of the European Avocet with ethological and psychological remarks. *Ardea 25,* 1-62.

Rand, A. L. (1943): Some irrelevant behaviour in birds. *Auk. 60,* 168-171.

Schloeth, R. (1958): Cycle annuel et comportement social du taureau de Carmargue. Mammalia, XXII, No. 1, p. 121-139.

Tinbergen, N. (1951): The study of Instinct. University Press, Oxford.

OBSERVATIONS ON CALF DISEASES IN KENYA

by

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1. DISEASE IN CALVES DUE TO SALM. DUBLIN: THE PROBLEM OF IMMUNITY

Introduction

During the last few decades, Kenya has attained the position of one of the great stock rearing countries of the world. Few realise the part played in this development by a Veterinary Department that has periodically been short of staff and finance and constantly assailed by the threat of major indigenous diseases that could rapidly, in the absence of constant vigilance, undermine the Colony's livestock industry.

In the European Settled Areas there are many dairy herds of pure bred imported British stock Jersey, Guernsey, Friesian, Shorthorn and Aberdeen Angus, comparable with the best in England. Whilst the heavy cost of importation has deterred many farmers the latter have attained nearly the same end by up-grading indigenous stock by the use of pure bred sires. The progeny is of high quality, both in milk and meat production. In addition to the dairy herds, some tracts of the settled areas are devoted wholly to ranching. Of the total cattle stock held in these areas, approximately 884,000, more than half are ranched.

The total area of farming land is approximately seven million acres. Much of the area is strictly equatorial. Altitudes vary between 4,000 and 9,000 feet. The average annual rainfall varies between 30 and 60 inches, with two rainy seasons. Temperatures vary according to the altitude. The climate on the more favoured farms, situated on the high lands, may be described as temperate.

Against such a background a survey of the causes of mortality in calves during the first six months of life provides certain points of interest, which may be of some value to tropical and subtropical countries where the cattle industry is less advanced than in Kenya. It is generally believed that, in this country, the average calf mortality is 25 per cent. It is known that, at times on some farms, this figure may be doubled. An analysis of data from 11 farms gave the figure 28.5 per cent. The methods of rearing calves varies considerably among farms. It has been stated by veterinarians in Kenya, that inadequate or faulty management is the root cause of calf mortality. This is a statement for which no proof exists. There have been severe losses when management conditions were excellent and moderate or comparatively little loss in calves reared casually. Even in calves running with their dams on ranches or under semi-ranched conditions, that might be considered ideal, considerable calf mortality may occur periodically. The determining factor would seem to be, not the conditions under which the calves are kept but, the nature and virulence of the infection that may appear quite spontaneously on a farm and spread to adjacent farms. Little is known about the epizootiology of such infections.

The purpose of this survey was to determine the nature of the infections and the means which could be economically adopted to reduce the deplorably high incidence of calf mortality. On the 33 farms upon which the survey was conducted, the following diseases were found to be the main causes of loss, viz. white scour (colibacillosis), calf paratyphoid (*Salmonella dublin*), pneumonia, anaplasmosis and a form of glomerulo-nephritis apparently unassociated with a specific infection. On one farm, or on a group of adjacent farms, white scour might account for the majority of losses and smoulder on the premises for years. On other farms, calf paratyphoid behaved in the same manner, whilst calf pneumonia had an almost ubiquitous distribution, though it was more periodic in its appearance.

The most pressing need was shown to be the control of calf paratyphoid due to *Salm. dublin,* which was spreading rapidly in the country (1950). Of 90 strains of salmonella isolated from cases of calf paratyphoid during this investigation, 83 were typed as *Salm. dublin* and the remainder as *Salm. typhi-murium.*

In Kenya, the use of calf paratyphoid vaccine prepared from *Salm. dublin* seems to date from 1927. Daubney then investigated, " the excessive mortality among calves three weeks to three months of age in many of the dairy herds in Kenya ", and found *Salm. dublin,* not infrequently associated with anaplasmosis, to be the chief cause. He thought that the latter infection was the factor precipitating many outbreaks of calf paratyphoid. This worker initiated vaccination of calves at risk on infected farms. The vaccine was prepared from four strains of *Salm. dublin,* one strain of *E. coli* and two strains of *Salm. typhi-murium,* all isolated from calves in Kenya. Each stock strain was maintained on agar slants stored at 5°C. Fresh sub-cultures of each strain on agar slants were seeded into flasks of ordinary broth pH 7.4, one strain to each flask, and these were incubated for 48 hours at 37.5°C. Formalin was added then to all flasks in the proportion of 5 ml. per litre and the contents of the flasks pooled. The mixture was incubated for 24 hours. This constituted the bulk suspension which was stored at 5°C. Vaccine was prepared from the concentrate by the addition of 1.5 litres to 6 litres of normal saline to which 30 ml. formalin had been added. The density of this vaccine was about one half opacity tube No. 1. Calves received 1 ml. of the vaccine subcutaneously at or shortly after birth. The strains of *E. coli* and *Salm. typhi-murium* were added as a possible means of control against the disease caused by these organisms. He concluded that, while the vaccine met with some success on some of the smaller farms, the results were disappointing in heavily infected herds. It proved difficult to assess the immunizing value of the vaccine in calves. He vaccinated a number of healthy calves and challenged them later with massive amounts of *Salm. dublin* culture given by mouth; they did not react, nor did a suitable number of control calves of the same age group. Nevertheless, in spite of failure to prove the worth of this vaccine, it was issued until the work now recorded was commenced in 1950.

Henning (1953) commented on the prevalence of the disease in South Africa and experimented with a formalinised alum adjuvant vaccine at least 40,000 times richer in bacterial substance than the Kabete vaccine. This vaccine protected 80 per cent. of vaccinated mice, challenged with an equal number of controls, in which the mortality was 87 per cent. Large numbers of mice were used to provide accurate statistically significant evidence of the immunising value of the vaccine. In calves vaccinated twice at a seven day interval and later challenged by massive doses of culture given

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by mouth, the results were not so promising. To quote Henning, "although the immunised calves undoubtedly suffered less from the challenge infection than the controls, the test cannot be regarded as satisfactory, and no definite results can be drawn from the results obtained". Nevertheless, field trials showed that this vaccine gave excellent results in the control of *Salm. dublin* infection of calves at risk on farms throughout the Union, even if it was, "admitted that the immunity is of low grade and that vaccination cannot be relied on entirely to prevent symptoms or even death from paratyphoid". Henning showed that H agglutinins against *Salm. dublin* were present in high titre in the sera of calves seven days after vaccination and that it was possible to boost titres to very high levels by re-vaccination at seven day intervals. In calves vaccinated twice, titres remained at this level for about four weeks. In calves vaccinated again 30 days after the second vaccination, H agglutination titres were enhanced still further and, in many cases, remained at the new level for four months. The O agglutination titres of these calves was negligible or nil.

The present paper records experiments at Kabete designed to evaluate the immunising value of the standard paratyphoid vaccine and to compare this with vaccines prepared by other methods.

Experimental

1—In Rabbits :

(*a*) Susceptibility of the rabbit to *Salm. dublin* culture:

The strain of *Salm. dublin* used in this experiment, labelled K.65, was obtained through the courtesy of the National Collection of Type Cultures. This culture was subcultured in peptone water on receipt and the 18 hour growth planted on agar. A smooth colony was selected for further work and subcultured on agar slant. The antigenic structure of this culture was examined and found to be somatic — I, IX, XIII: flagellar — g, p.

The culture was again subcultured on agar slants, incubated for 18 hours, washed off with N.S.S. and the suspension adjusted to No. 1 opacity tube. Three young rabbits were each inoculated intravenously with 0.1 ml. 10^{-2} dilution of the suspension. Blood (0.01 ml.) was taken from the ear vein of these rabbits at 5, 24 and 48 hours after inoculation, and three agar plates sown with each sample. The readings were: swarming at five hours, average twelve colonies at 24 hours and nil at 48 hours, *Salm. dublin* alone being isolated. No illness developed during one month's observation and *Salm. dublin* was not isolated from faeces. The latter were examined at four day intervals during this period. The rabbits were destroyed then and cultures made on D.C.A. plates from liver, mesenteric lymph gland, spleen, kidney and ileum yielded no salmonella. It was concluded that the rabbit is not susceptible to such an experimental infection.

Four rabbits were inoculated intradermally each with 0.1 ml. 10^{-3} dilution 18 hour broth culture K.65. This caused a localised oedema at the site of inoculation, which commenced to recede at the 36th hour, until, at the 72nd hour only a lentil sized nodule was apparent within the skin. This disappeared within one week. These rabbits were destroyed one month after inoculation and no salmonella were found on examination of the tissues. Four rabbits were given *Salm. dublin* K.65 strain broth

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culture *ad lib* in the mash for ten days. The organism was not recovered in the faeces during this period and no disease was produced.

Five rabbits were each inoculated subcutaneously with 0.1 ml. 18 hour broth culture K.65. Twenty days later their sera were tested against H and O antigens prepared from the homologous culture. All gave H agglutination titres of 1/640: against O antigen the titres were: 1/60 (2), 1/320 (3). In each of these rabbits along with four controls were challenged intradermally with 0.1 ml. 18 hour broth culture K.65 strain. A severe local inflammatory lesion, about one inch in diameter, developed within 24 hours in the rabbits previously inoculated with culture. This abated in severity within 7-10 days and was slowly succeeded by a local granuloma which sloughed about 14 days later. Healing eventually occurred. In control rabbits, the local lesion was mild in comparison. It regressed rapidly, until at three days it was visible only as a firm, lentil sized nodule, which was totally absorbed within a few days. It will be noted that the test inoculum was approximately 1,000 times that used in the rabbits previously inoculated by this route. One rabbit from each batch was killed 72 hours after challenge. Films prepared from the cut surface of both types of lesions and suitably stained showed a striking difference. In the control rabbit, organisms were somewhat scanty in distribution whereas, in the other rabbit, organisms swarmed and were packed densely within phagocytes. Giemsa stained skin sections emphasised this difference. It seems reasonable to assume that the skin reaction in previously inoculated rabbits is an immunity phenomenon. As rabbits could not be infected by the subcutaneous or intravenous routes with living cultures or by feeding the same material, we had no alternative to the intradermal test as a measure of immunity in rabbits vaccinated by various vaccines, for comparison with the levels of immunity attained in rabbits vaccinated with the standard Kabete vaccine. Various vaccines for rabbit test were now prepared from *Salm. dublin* K.65 strain, viz. heat-treated, phenolised and formalinised. These vaccines were prepared from a common antigen, viz. Roux flasks containing nutrient agar pH 7.4 were seeded with 18 hour broth culture K.65 strain, incubated 18 hours at 37.5°C. the growth washed off with normal saline and the suspension adjusted to No. 5 opacity tube. An aliquot was formalinised at 0.1 per cent.; this low dilution which sterilised the vaccine after 24 hours incubation at 37.5°C. was selected on the grounds of an observation (Pons, 1942) that greater antigenicity of vaccines is attained with a low dilution of formdalin than with the conventional one per cent. dilution.

Heat treated vaccine was prepared by heating an aliquot at 60°C. for one hour. This killed the organisms. Another was phenolised at 0.5 per cent. to constitute the phenol vaccine. "Standard" vaccine was taken from stock. Young rabbits were selected for vaccination with the various vaccines so prepared. In addition, live broth culture K.65 strain was used as a vaccine. The heat treated vaccine was given to rabbits in a single dose and also in increasing doses at five day intervals, viz. 0.25 ml., 0.5 ml., 0.75 ml., etc., to a total of 19.5 ml., the intravenous route being used for inoculation. Rabbits were bled at intervals after vaccination and the serum agglutinins read against K.65 H and O antigens prepared by standard methods. Agglutination tests were done by the Dreyer technique to obtain both intermediate and end points. Table 1 gives the results. Titres are expressed as the denominator of the conventional reading. One week after the last reading, when all serum titres were nil, these rabbits

were tested intradermally with 0.1 ml. 18 hour broth culture K.65 strain. With three exceptions, all gave as strong a reaction as that noted in those rabbits given live culture, and tested 20 days later when the titres were 0:320/640:H:640. The three exceptions were, one rabbit given 0.1 phenol vaccine, and one rabbit given 0.1 ml. standard Kabete vaccine. Neither of these reacted. In the third rabbit given 0.1 ml. heat treated vaccine, the reaction was slight and fleeting. Four control rabbits were tested in the same way and gave the reaction previously noted.

TABLE 1

No.	Vaccine	Dose ml.	Readings, Days after Vaccination					
			14		26		40	
			H	O	H	O	H	O
1	Phenol vac.	1.0	60	250	20	250	nil	nli
2	" "	0.1	50	20	10	nil	nil	nil
3	Standard	1.0	20	20	nil	nil	nil	nil
4	Kabete	0.1	20	20	nil	nil	nil	nil
5	"	1.0	50	20	nil	nil	nil	nil
6	"	0.1	25	20	nil	nil	nil	nil
7	Heat treated	1.0	80	20	nil	nil	nil	nil
8	" "	1.0	250	20	nil	nil	nil	nil
9	" "	0.1	20	100	nil	nil	nil	nil
10	" "	0.1	20	100	nil	nil	nil	nil
11	K.65 broth culture	1.0	500	250	nil	nil	nil	nil
12	" " "	1.0	125	250	nil	nil	nil	nil
13	" " "	0.1	250	250	nil	nil	nil	nil

			14		20		30		40	
			H	O	H	O	H	O	H	O
14	Standard	5.0	80	40	20	40	20	20	nil	nil
15	Kabete	5.0	80	40	20	40	20	20	nil	nil
16	Formalinised	5.0	80	600	250	600	400	20	nil	nil
17	"	5.0	400	1500	100	1250	400	20	nil	nil
18	"	1.0	40	1250	250	1250	800	800	nil	nil
19	"	1.0	600	60	400	800	1250	20	nil	nil
20	"	0.5	400	800	250	2500	400	2500	nil	nil
21	"	0.5	250	800	125	1250	800	800	nil	nil
22	"	0.5	100	1250	80	600	800	2500	nil	nil
23	"	0.5	250	1250	20	2500	800	1250	nil	nil
24	"	0.1	200	2500	200	1250	800	20	nil	nil
25	"	0.1	125	800	400	1250	800	20	nil	nil

			14		30		45	
			H	O	H	O	H	O
26	Heat treated in increasing dosage		1250	1250	1250	600	600	nli
27	" " "		1250	1250	1250	600	600	nli

2—In Mice :

Mice were found to be highly susceptible to experimental infection with strain K.65. Experiments at Kabete were hampered by an apparently ineradicable subclinical infection of the stock mice with *Salm. typhi-murium* which was exacerbated when such mice were inoculated with *Salm. dublin.* In attempts to determine the LD_{50} of an 18 hour broth culture of strain K.65 for mice, for the challenge of vaccinated

mice, difficulty was met with immediately. The results of a typical experiment are shown below. Mice were inoculated in batches of twenty with serial ten-fold dilutions of 18 hour broth culture, the inoculum being 0.1 ml. per mouse intraperitoneally.

TABLE 2

Dilution	Bacterial Count	No. of Deaths	% Deaths
10^{-2}	Uncountable	20	100
10^{-3}	"	20	100
10^{-4}	"	20	100
10^{-5}	Approx. 2,500	14	70
10^{-6}	240	4	20
10^{-7}	47	3	15
10^{-8}	15	nil	nil
10^{-9}	2	nil	nil

It would seem, therefore, that the LD_{50} was approximately 0.1 ml. of 10^{-5} dilution. Bacterial counts were made on agar plates seeded with 0.1 ml. of the various dilutions. Deaths in mice occurred between three and ten days after inoculation, and varied directly with the dose of culture. The liver and spleen of all mice that died were sown in selenite F broth tubes, incubated 24 hours, and then plated on D.C.A. Sixteen per cent. of all mice that died yielded both *Salm. dublin* and *Salm. typhimurium*. The survivors were all killed and *Salm. dublin* recovered from the tissues of them all by the technique described.

A group of 20 mice was inoculated intraperitoneally each with 0.1 ml. 10 dilution 18 hour broth culture K.65 strain. Forty-eight hours later, at the peak of illness, all were treated with sulphathiazole sodium (33 per cent. solution) for three successive days, each mouse receiving 0.1 ml. of the drug twice daily by the intraperitoneal route. This treatment effected a cure but did not sterilise the tissue, as was proved later at autopsy of a few of the mice. After a rest period of one month, the original inoculation was repeated in the remainder of this group. No reaction was observed in these mice following this inoculation. The nature of this phenomenon was investigated. It was found that, if films were made, at ten hour intervals, from the peritoneal exudate of such mice and stained by Giemsa, marked phagocytosis was present with intense propagation of the organism in the exudate; at 20 hours phagocytosis was at a maximum with little propagation of the organism; ten hours later the clearance of organisms was still more marked, until at 40 hours it was complete. In similar readings made in a group of normal mice given the same inoculation, phagocytosis was mild with intense propagation of the organism in the exudate, this picture progressing to the point of failure of phagocytes to hold the infection, which swarmed until death. The phenomenon noted in mice infected, and later treated, is obviously related to immunity.

During a recent visit to England, the opportunity arose of examining the immunising value of *Salm. dublin* vaccines in mice known and proved to be perfectly free from salmonella infections. The vaccines tested were prepared in the same way as those used in previous work with rabbits, viz. Kabete standard vaccine, and the formalinised vaccine adjusted at No. 5 opacity tube. Groups of 50 mice were vaccinated with each vaccine at a flat dose of 0.2 ml. Fifty mice were each inoculated intraperitoneally with 0.1 ml. K.65 strain 18 hour broth culture and treated with sulphathiazole sodium (33 per cent.), to form a group of " immune " mice. The three

groups of mice were challenged along with 50 normal mice six weeks after vaccination; the challenge was 0.1 ml. 10^{-2} dilution 18 hour broth culture K.65 strain given intraperitoneally. The results were clear cut, viz. 100 per cent. mortality in controls within five days; 60 per cent. protection in mice given Kabete standard vaccine; 96 per cent. protection in mice given the stronger vaccine; 100 per cent. protection in "immune" mice. Mortality among vaccinated mice occurred within the period 5 to 10 days after challenge and no deaths occurred during a further period of observation of one month.

3—In Cattle :

Four calves aged 8 to 10 weeks were each given one quarter litre 18 hour broth culture K.65 strain daily in the milk ration for three days. None showed any reaction, febrile or otherwise, during two months observation. Using the selenite F/D.C.A. technique, the organism could not be recovered on bi-weekly examination of faeces. Two of these calves were destroyed at the end of two months; neither showed any lesions indicative of a salmonella infection and the organism could not be isolated from liver, spleen and mesenteric lymph glands. Two calves of the same age group were each inoculated intravenously with 0.1 ml. of the same culture. They developed acute salmonella disease to which they succumbed 4 and 6 days after inoculation, the organism being recovered from all tissues on autopsy. Two yearling steers were each inoculated intravenously with 1.0 ml. of the same culture and showed no illness over a period of one month nor could the organism be isolated from the blood or faeces on daily examination for ten days following inoculation.

The agglutinogenic response of calves vaccinated with standard Kabete vaccine and a vaccine formalinised at 0.5 per cent. and adjusted at No. 4 opacity tube was examined. The latter vaccine was prepared from a recently isolated field strain of *Salm. dublin* labelled Soysambu. An outbreak of calf paratyphoid due to this organism had been smouldering on the estate of this name for some months and neither the Kabete vaccine nor an autogenous vaccine prepared on the same lines from the local strain had proved of any value in controlling the persistent incidence of disease. Calves had been vaccinated at or shortly after birth and the disease appeared in calves 10 to 16 weeks old.

Seventeen calves were used in this experiment, either pure bred Guernsey or Hereford breed between 10 and 20 days old. These calves were divided into four batches of three and one of five. Batch 1 was vaccinated with one dose (5.0 ml.) Kabete vaccine, batch 2 was given the same dose at approximately monthly intervals over a period of three months, and batches 3 and 4 were vaccinated in the same fashion with Soysambu vaccine. The agglutination titres of calves of each batch were read against H and O antigens of both K.65 and Soysambu strains at stated intervals after vaccination. The Dreyer technique was used throughout. Tables 3-6 give the results. The sera of the batch of unvaccinated calves (5) gave consistently negative titres against all antigens on parallel readings.

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TABLE 3

Effect of giving one dose of 5 ml. of standard paratyphoid vaccine subcutaneously to each of three calves on 12.5.53.

Calf Number	H Antigen K.65	H Antigen Soysambu	O Antigen K.65	O Antigen Soysambu	Date of Agglutination Test
1	1/25	1/25	neg.	neg.	12.6.53
2	1/25	neg.	neg.	neg.	"
3	1/25	neg.	neg.	neg.	"
1	neg.	neg.	neg.	neg.	12.7.53
2	neg.	neg.	neg.	neg.	"
3	neg.	neg.	neg.	neg.	"

TABLE 4

Effect of giving three doses of 5 ml. of standard paratyphoid vaccine subcutaneously to each of three calves on the following dates: 17.12.52, 21.1.53 *and* 11.3.53.

Calf Number	H Antigen K.65	H Antigen Soysambu	O Antigen K.65	O Antigen Soysambu	Date of Agglutination Test
4	1/3000	1/2500	1/30	1/30	14.4.53
5	neg.	neg.	neg.	neg.	"
6	1/600	1/400	neg.	neg.	"
4	1/400	1/400	neg.	1/40	14.5.53
5	1/125	1/60	neg.	neg.	"
6	1/60	1/60	neg.	neg.	"
4	1/300	1/300	neg.	1/40	11.6.53
5	neg.	neg.	neg.	neg.	"
6	1/60	1/25	neg.	neg.	"
4	1/125	1/125	neg.	neg.	13.7.53
5	neg.	neg.	neg.	neg.	"
6	neg.	neg.	neg.	neg.	"
4	1/25	1/25	neg.	neg.	11.8.53

As many farmers had doubts as to the efficacy of vaccination against calf paratyphoid due to *Salm. dublin,* sulphadimidine was being used by them quite largely in treatment, but with very doubtful results. We investigated the sensitivity of four strains of *Salm. dublin,* viz. N.C.T.C. strains K.65 and C.236 and two recently isolated Kenya field strains against the sulphonamides: sulphamerazine, sulphadiazine, sulphanilamide, sulphathiazole, sulphapyridine, sulphadimidine, succinylsulphathiazole, phthalylsulphathiazole, benzylsulphanilamide, succinylsulphathiazole and dapsone. The technique used was that of Harper and Cawstone (1945). Nought point one ml. 10^{-3} dilution 18 hour broth culture of each strain was tested separately against two concentrations of each drug, viz. 1 and 5 mgm. per cent. The results were read after 24 and 48 hours incubation of plates. All four strains were fully sensitive to the lower concentration of sulphathiazole and to the higher concentration of this drug as well as sulphapyridine, phthalylsulphathiazole and sulphadiazine. Strain C.236 was also fully sensitive to sulphamerazine. All other sulphonamides tested were of no appreciable value.

TABLE 5

Effect of giving one dose of 5 ml. of Soysambu vaccine subcutaneously to each of three calves on 21.3.53.

Calf Number	H Antigen		O Antigen		Date of Agglutination Test
	K.65	Soysambu	K.65	Soysambu	
7	1/250	1/250	neg.	1/60	21.4.53
8	1/250	1/250	1/30	1/60	»
9	1/250	1/125	1/60	1/25	»
7	neg.	1/30	neg.	neg.	22.5.53
8	neg.	neg.	neg.	neg.	»
9	neg.	1/30	neg.	neg.	»
7	neg.	neg.	neg.	neg.	22.6.53
8	neg.	neg.	neg.	neg.	»
9	neg.	neg.	neg.	neg.	»

TABLE 6

Effect of giving three doses of 5 ml. of Soysambu vaccine subcutaneously to each of three calves on 11.3.53, 14.4.53 *and* 12.5.53.

Calf Number	H Antigen		O Antigen		Date of Agglutination Test
	K.65	Soysambu	K.65	Soysambu	
10	1/125	1/2500	neg.	neg.	11.6.53
11	1/250	1/2500	neg.	neg.	»
12	1/250	1/500	neg.	neg.	»
10	1/25	1/250	neg.	neg.	13.7.53
11	1/50	1/250	neg.	neg.	»
12	1/50	1/25	neg.	neg.	»
10	neg.	1/25	neg.	neg.	11.8.53
11	neg.	1/25	neg.	neg.	»
12	neg.	1/25	neg.	neg.	»

The issue of a new type of calf paratyphoid vaccine to the field was now undertaken. This was prepared from *Salm. dublin* K.65 strain and a strain of the organism isolated from a fatal case of the disease on infected premises, i.e. the vaccine was partly autogenous. Each strain was grown in broth pH 7.4, incubated 18 hours at 37.5°C., and a loopful of this culture was sown on agar plates and incubated in the same way. Smooth colonies were selected for vaccine seed and the total absence of roughness checked by the acriflavine precipitation test. (It is worth noting that in all the *Salm. dublin* cultures that we have examined and maintained in this Laboratory during the course of the investigation, none has ever exhibited any tendency to develop roughness). The selected seed material was sown in Roux flasks containing nutrient agar. These were incubated for 18 hours at 37.5°C. The growth was then tested again for any possible roughness. Passing this test, growth was washed off with 0.2 per cent. formol-saline and the suspension adjusted to No. 5 opacity tube. The harvested vaccine was stored at 37.5°C. for 48 hours and sterility and biological tests carried out, viz. 10 ml. of the vaccine was sown in two lots of 50 ml. nutrient broth, one incubated for one week at 37.5°C. under aerobic conditions and the other in the same way under anaerobic conditions. Twenty mice were each inoculated intra-

peritoneally with 0.25 ml. vaccine. If cultures remained sterile and mice showed no reaction, the vaccine was issued. It will be noted that this vaccine was purposely made much richer in bacterial substance than the original standard Kabete vaccine. The reason for this step was as follows:

Experiments in rabbits showed that better agglutination titres were obtained with a vaccine of this type than with the relatively weak Kabete vaccine. Immunity tests in mice indicated even more strongly the comparative worth of the two types of vaccine. In experiments with calves, tables 4 and 6 show that when calves of the same age group are vaccinated thrice at monthly intervals, the agglutination titres against H antigen remain at a reasonable level up to one month after the last vaccination, with an appreciable value in the second month. Tables 3 and 5 show that in calves of the same age group vaccinated with a weak vaccine agglutination titres are feeble in comparison with those obtaining with the stronger vaccine; the latter tend to persist to a time when the former have totally disappeared, and in addition, the stronger vaccine gives some O agglutination. An interesting feature of these results, which might have been explored further if more calves had been available, was that slightly better H titres were noted, both against K.65 and Soysambu antigens, in calves vaccinated with three doses of standard Kabete vaccine, and over a slightly longer period; a result offset, however, by the failure of calf 5 to give any titre.

Instructions issued with the vaccine were that calves would be vaccinated each with 5 ml. subcutaneously at one month and two months of age, with a recommendation that, in known infected premises, a third vaccination at three months was desirable. It was also advised that vaccine be used within a period of one week of manufacture. There was no dearth of infected farms on which to test the value of the vaccine. No farmer would agree to vaccinate one half of the calves at risk and leave the remainder as controls. We had no option but to undertake wholesale vaccination. It soon became apparent that the incidence of disease dropped steeply on infected farms, where vaccination was being practised according to instructions. This was particularly noticeable on farms, where the disease had been smouldering for many months with a fluctuating mortality. A further, if indirect, proof of the value of the vaccine was seen on certain farms where, following vaccination, the incidence of disease ceased and further vaccination of calves was disregarded. Such farmers learned in the school of hard experience, when it became apparent that the vaccine had undoubted value in the control of the disease, and that, in the absence of vaccination, continued losses were inevitable. On one farm, a farmer failed to follow instructions and used vaccine six months after the date of manufacture. Three of 16 calves vaccinated died within a few hours with symptoms of acute shock and a varying degree of the same upset was exhibited by the remainder. We were well aware, when we laid down the instructions for the use of the vaccine, that its keeping properties were probably limited by the gradual release of bacterial endotoxins. To avoid this risk, we had advised the almost immediate use of the freshly prepared vaccine.

Henning (loc-cet) working with a similar vaccine, work then unknown to us, met with a similar experience in vaccination of calves. He showed (1953) that this difficulty could be overcome by the addition of an alum adjuvant to the vaccine, and that such a vaccine had an undoubtedly better immunising value than a vaccine not incorporating the additive. With this information and from this date, we have issued an alum

adjuvant vaccine to the field. We have not altered the basic formula of the vaccine. We have simply added alum adjuvant to the concentration recommended by Henning. We have not again encountered untoward effects from vaccination with this vaccine.

Discussion

The problem of immunity in salmonella disease is complex. The immense volume of work that has been done on the problem of immunity against *Salm. typhi* infection without attaining unequivocal results, emphasises this statement. Topley and Wilson (1955) express some doubt of typhoid vaccines as a whole and state, "anti-typhoid vaccination carried out by the best technique at present available would form a poor substitute for the ordinary methods of sanitary control as applied to a population exposed to a severe and continuous risk".

Greenwood, *et alia* (1931) in studies on herd immunity have shown what happens when mice given *Salm. typhi-murium* vaccine are introduced into a mouse population infected with this organism. Morbidity and mortality was slightly lessened in vaccinated mice; they survived the infection somewhat longer than non-vaccinated mice. It was also shown that the somatic antigen was alone concerned with such immunity as was seen.

Levi (1949) and Gibson (1957) have noted a considerable, usually high, titre of flagellar agglutinins in the sera of goat populations naturally infected with *Salm. dublin*: the titre of somatic agglutinins was negligible. These goats gradually built up their own immunity against the infection and survived. The question may be posed whether H titre response had any significance in the development of this immunity. It is well known that, in the preparation of *Salm. typhi* vaccine, smooth and virulent strains of the organism are of key importance; also that an avirulent strain is almost as worthless as a wholly rough strain.

It may not be logical to apply such premises to the search for a vaccine against *Salm. dublin* infection of calves; they have been a valuable guide, none the less. The work recorded in this paper has been conducted mainly with one strain of *Salm. dublin*, viz. K.65. Its virulence for calves by intravenous inoculation was proved but, when an attempt was made to infect calves with the same material by mouth, a route that must be accepted as the normal portal of entry in field infections, no disease ensued. Similarly, Henning (1953) and Daubney (1927) using recently isolated and presumably virulent field strains of *Salm. dublin* generally failed to produce active symptoms of clinical disease by feeding culture: perhaps even more important, the organism inoculated was only occasionally isolated and no specific lesions of the internal organs, e.g. liver, were produced. It is this inherent difficulty that is the stumbling block to any critical appraisement of the value of the vaccine. Yet, while calves are very susceptible to an intravenous inoculation of *Salm. dublin* and yearling cattle wholly refractory to a very much larger dose, there must lie, between these extremes, a means at which a 50 per cent. end point of infection could be determined. We had hoped to carry out blood clearance tests in vaccinated calves of this, as yet undetermined age group, but sufficient have not been available. It has been shown in this work that mice are very susceptible to inoculation with cultures of K.65. Whether the results obtaining from immunity experiments in mice can be accepted as a portent of immunity in the specific host, e.g. in calves, is again debatable. That a strong degree of immunity can be conferred in mice by vaccination is proved. In mice, the immunity

phenomenon would seem to depend on the simple mechanism of opsonic activity. In vaccinated rabbits later challenged, the same phenomenon is noted; the infective dose is firmly held by an intensive phagocytic reaction at and around the zone of infection. It would appear also that this immunity is not related to O or H agglutinins, as immunity was challenged when serum titres against both antigens were nil. In vaccinated cattle, it would almost appear that persistence of H titres has some significance in immunity; thus in calves vaccinated with one dose of standard Kabete vaccine, H. titre is negligible and disappears rapidly and such a vaccine in single dose has proved of doubtful value in field control of the disease. On the other hand, in calves given three doses of a vaccine richer in antigenic substance, H titres persist for some time after the last vaccination and such a vaccine, when put to field trials, brings a reasonable level of control. Despite this result, the use of such a vaccine in the field is not really justifiable. Eradication of the sources of infection should be the aim. The carrier rate of cows in infected herds in Kenya is probably high, though this has not been examined in the present survey.

Conclusions

A formalinised vaccine prepared from a smooth virulent strain of *Salm. dublin* and rich in bacterial substance gives a reasonably efficient protection to calves at risk against this infection. As immunity is apparently of short duration, monthly vaccination at one and two months of age is advised. In badly infected herds, a third vaccination may be necessary. The addition of an alum adjuvant to this vaccine controls the risk of shock in vaccinated calves.

The standard Kabete calf paratyphoid vaccine prepared from local, Kenya strains and in use until 1954, has consistently failed to control outbreaks of the same disease of calves in Kenya. The main reason would seem to be that this vaccine is poor in bacterial substance and that it is given only once, at or shortly after birth so that, at the peak of the incidence of the disease, viz. in calves about three months old any residual immunity is insufficient to protect against a field infection.

The serological response of young calves vaccinated either with the strong or weak vaccine is the production of flagellar agglutinins. The somatic agglutinin response is negligible. In calves vaccinated once with the weak vaccine, the flagellar agglutinins are poorly developed and disappear rapidly from the serum, whereas, in calves vaccinated thrice at monthly intervals with the stronger vaccine, such agglutinins remained at a fairly high titre over three months and persisted at a lower level for one month after the last vaccination. This response to vaccination may have some significance in the evaluation of immunity in calves.

In rabbits vaccinated once with the strong vaccine, somatic and flagellar agglutinins develop in the serum within ten days of vaccination. Both agglutinins disappear from the serum between the 30th and 40th day after vaccination. In rabbits vaccinated once with the weak vaccine, both flagellar and somatic agglutinins are at insignificant levels and disappear even more rapidly; phenolised and heat treated vaccines gave the same results.

The relative value of both vaccines has been assessed in immunity tests of groups of vaccinated mice. On a challenge, which killed 100 per cent. controls rapidly, the strong vaccine gave a much better protection than the weak.

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Acknowledgments

It is a pleasure to acknowledge the valuable help given by Mr. E. J. Bishop, F.I.M.L.T. and Mr. W. A. Ashford, A.I.S.T. in the prosecution of the work recorded in this paper. Special thanks are due to Mr. H. I. Field, M.Sc., M.R.C.V.S., for his kindness and generosity in granting me laboratory facilities for some weeks at the Veterinary Investigation Centre, Cambridge.

The paper is published with the permission of the Director of Veterinary Services, Kenya.

REFERENCES

Daubney, R. (1927): *Vet. Rec.*, *7*, 38, 793.
Gibson, E. A. (1957): *Vet. Rec.*, *67*, *44*, 1026.
Greenwood, M., Topley, W. W. C. and Wilson, J. (1931): *J. Hyg., Camb.*, *31*, 484.
Henning M. W. (1953): *Onderstepoort J. vet. Sci.*, *26*, i, 25.
Levi, M. L. (1949): *Vet. Rec.*, *61*, 555.
Pons, R. (1942): *Rev. Immunol.*, *7*, 222.
Topley, W. W. C. and Wilson, G. S. (1955): Principles of Bacteriology and Immunity, 4th edit. revised by Wilson, G. S. and Miles, A. A., Ch. 69 p.1751.

THE EFFECT OF ENVIRONMENTAL TEMPERATURE ON THE RECTAL TEMPERATURE OF FATTENING PIGS

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In warm blooded animals the body temperature usually remains practically constant, even though the temperatures of the surroundings vary. This constancy of body temperature is effected by a continuous balancing of the various factors which produce or give off heat. The pig has a less efficient thermo-regulatory mechanism than some of the other domesticated animals, and so its body temperature is not as stable as, for example, that of the cow or sheep. In fact, the body temperatures of healthy pigs can vary over a considerable range. After examining the findings of various authorities, Findlay (1950) quotes a range of rectal temperature for the pig from 98.3° to 104°F. Other workers who have drawn attention to the wide variations which are encountered include Miller and West (1953) who give 100.9° to 104.9°F. as the normal range within which a pig need not be regarded as ill, with 103.5°F. as the temperature which can be regarded as normal for ordinary practical purposes, and Murray Pullar (1949) who studied the records of 88 normal pigs of various ages from two to eight months, and found that the range was from 97.2°F. to 106.6°F., with a mean of 102.3±0.413°F.

Most observations on the changes in body temperature which occur at varying environmental temperatures have been made by keeping pigs for relatively short periods in small temperature controlled chambers. From observations made in such a psychrometric room on the behaviour of male Berkshire pigs of 130 lb. average weight exposed for periods up to seven hours in length to hot atmospheres of different temperatures but the same relative humidity of 65%, Robinson and Lee (1941) found

that at an air temperature of 70°F., the mildest degree of heating used, the rectal temperature fell at first, but later rose somewhat above normal. With intermediate degrees of heating up to 90°F. the rectal temperature rose, but progressed towards some kind of equilibrium. With higher degrees of heating up to 110°F., the rectal temperature rose with increasing rapidity without showing any indication of establishing an equilibrium. They concluded that below a dry bulb temperature of 85°F. environmental temperature did not have any regular or well defined effect on rectal temperature. Heitman and Hughes (1949) exposed pigs in two weight ranges, from 70 to 144 lb. and 166 to 260 lb., to environmental temperatures from 40°F. to 115°F. for short periods, and showed that as the air temperature rose the rectal temperature increased. The increase was more marked at the higher temperatures from about 70°F. in the heavier pigs and about 80°F. in the lighter group. The magnitude of the increase was also greater in the heavier pigs.

There appear to be few published references to the changes in body temperature which occur when pigs are kept for long periods at different environmental temperatures within the range normally accepted as suitable for pigs. Johnston *et al.* (1956) conducted an investigation into the interaction of temperature and feeding upon carcass and feeding characteristics of pigs in which the pigs were kept in controlled temperature chambers for periods varying from 26 to 32 days. The records of the control pigs on unsupplemented diets showed that at an environmental temperature of 58°F. the average body temperature was 102.6°F. and at 80°F. it was 103.9°F. Twelve pigs were kept at each environmental temperature level. In other experiments the average body temperatures were 103.1°F. for 13 pigs kept at 50°F. and 103.6°F. for 17 pigs kept at 90°F.

TABLE 1

Pigs from 9-16 weeks of age

Experiment No.	No. of pigs in each pen	Body Temperature (°F)			Environmental Temperature (°F)			Relative Humidity (%)		
		Warm pens	Cool pens	Diff. (W-C)	Warm pens	Cool pens	Diff. (W-C)	Warm pens	Cool pens	Diff. (C-W)
1	2	102.3	101.8	0.5	60	51	9	81	84	3
2	2	102.4	101.5	0.9	62	51	11	73	80	7
3	3	102.1	101.6	0.5	60	54	6	73	75	2
4	2	102.5	101.9	0.6	60	52	8	79	74	—5
5	2	102.2	101.5	0.7	62	52	10	75	84	9
6	2	102.3	101.7	0.6	60	50	10	79	84	5
Average		102.3	101.7	0.62*	60.7	51.7	9*	76.7	80.2	3.5†

* Difference in the means significant at the 1% level of significance.

† Difference in the means not significant.

As there is a shortage of information on the effect which keeping pigs for long periods at different environmental temperatures has on their body temperatures, and because of the known importance of environmental temperature on the health and productivity of pigs, the experiment reported here was designed to investigate the effects of two environmental temperatures, both within the usually accepted range of normality, on the body temperature of pigs for two periods of eight weeks duration each from 9 to 16 and 17 to 24 weeks of age inclusive respectively.

Experimental Method

The work was carried out during the winter months and the pigs were housed in pens in a well insulated Danish type piggery. The sleeping area of each pen, where the pigs spent most of their time, was free from draughts and was covered by a low

TABLE 2

Pigs from 17-24 weeks of age

Experiment No.	No. of pigs in each pen	Body Temperature (°F)			Environmental Temperature (°F)			Relative Humidity (%)		
		Warm pens	Cool pens	Diff. (W-C)	Warm pens	Cool pens	Diff. (W-C)	Warm pens	Cool pens	Diff. (C-W)
1	2	102.3	102.1	0.2	62	52	10	70	76	6
2	2	102.2	102.0	0.2	62	51	11	79	84	5
3	3	102.5	102.1	0.4	63	55	8	77	80	3
4	2	102.4	102.0	0.4	65	54	11	74	79	5
5	2	102.5	102.0	0.5	61	54	7	80	81	1
6	2	102.3	102.1	0.2	61	52	9	79	82	3
Average		102.4	102.1	0.32*	62.3	53	9.3*	76.5	80.3	3.8*

* Difference in the means significant at the 1% level of significance.

wooden ceiling to which was attached an electic heating lamp. Each lamp was controlled by a thermostat, and these were set at 60°F. and 50°F. respectively in the warm and cool environment pens. Wet and dry bulb thermometers were placed in the sleeping compartments of each pen, and were read each morning as soon as the pigs commenced feeding.

The diet throughout consisted of weatings 45, barley meal 30, flaked maize 14½, fish meal 7½, dried grass meal 2½, vitamin supplement (A and D) ½, all parts by weight, compressed into cubes. The pigs were fed to appetite, the weight of the cubes fed to each pig being altered once or twice each week as required, up to a total of 6½ lb. of cubes per head per day. Feeding was twice daily at 8.30 a.m. and 4 p.m. The cubes were fed with water, allowing 3 lb. of water to each lb. of cubes. There was no other source of water.

The 26 pigs used were all purebred Large White hogs from virus pneumonia free herds purchased soon after weaning at 8 weeks of age. They were placed in the experimental pens, and allowed about one week in which to become accustomed to their new surroundings. Their body temperatures were taken daily during this period, although the findings were not recorded, so that the pigs became familiar with this procedure. The pigs selected were as even in size as possible, and, at the start of the experiments, the average body weights of the pigs placed in the cool and warm environmental pens were the same, namely 35 lb. The pigs were weighed once a week, they all grew at a reasonable rate, and did not show any abnormal signs during the experimental period. In both age ranges the pigs in the warm pens grew slightly more rapidly, the average weight increases in the 9 to 16 weeks age group being 55 lb. for the warm pens and 49 lb. for the cool pens, and for the 17 to 24 weeks range 77 lb. and 72 lb. respectively for the 8 week periods.

Results

Although the thermostats were set at 60°F. and 50°F. in the warm and cool environment pens the actual temperatures achieved were not constant, and varied according to the external environmental conditions. As these tended to affect both sets of pens to the same extent a temperature difference of 9° or 10°F. was maintained between them fairly constantly.

As can be seen from the tables the average temperatures for all the warm pens were 60.7°F. for the pigs from 9 to 16 weeks of age and 62.3°F. for the period from 17 to 24 weeks, and 51.7°F. and 53°F. respectively for the cool pens for the same age ranges. The higher temperatures recorded for the pens containing the older pigs were caused by the increased amount of body heat given off because of their larger body size. No special precautions were taken to control the relative humidity, and the figures were typical of the average conditions of the building. The relative humidities for the pens containing the younger pigs were 76.7% for the warm pens and 80.2% for the cool pens, the difference between them not being significant, and those for the pens with the older pigs were 76.5% and 80.3% respectively, this difference being significant at the 1% level of significance.

The average body temperatures of the pigs in the warm pens were greater than those of the pigs in the cool pens in the six repetitions in both age ranges. In the younger group the average of the temperatures of the pigs in the warm pens exceeded that of the pigs in the cool pens by 0.62°F., this difference being significant at the 1% level. In the older group the average of the temperatures of the pigs in the warm pens exceeded that of those in the cool pens by 0.32°F., this difference also being significant at the 1% level.

Although both results are significant it would appear from the greater difference in the averages of the body temperatures of the pigs kept at the two environment temperatures while they were young compared with the same pigs when older, that increasing age enabled them to maintain a more even body temperature. This might have been due to the fact that as the pigs grew the fat layer under the skin gradually developed in thickness and acted as an insulator against temperature changes.

Summary

In a series of 6 experimental repetitions 13 pigs were kept at environmental temperatures of about 50°F., and the same number at about 60°F. for a total of 16 weeks in each case. The results are given for two 8 week periods, from 9 to 16 and 17 to 24 weeks of age inclusive respectively. The average body temperatures of the pigs in the warm pens exceeded those of the pigs in the cool pens in all six repetitions in both age groups. In the younger pigs the average of the temperatures of those in the warm pens exceeded that of those in the cool pens by 0.62°F., this difference being significant at the 1% level. In the older group the average of the temperatures of the pigs in the warm pens exceeded that of those in the cool pens by 0.32°F., this difference also being significant at the 1% level.

REFERENCES

Findlay, J. D. (1950): *Bull Hannah Dairy Res. Inst.* No. 9, 98.
Heitman, H. (Jr.) and Hughes, E. H. (1949): *J. Anim. Sci., 8,* 171.
Johnston, E. F., Ellis, N. R. and Winchester, C. F. (1956): *J. Anim. Sci., 15,* 271.
Miller, Wm. C. and West, G. P. (1953): *Black's Veterinary Dictionary.* Third Edition, A. & C. Black Ltd., London.
Murray Pullar, E. (1949): *Brit. vet. J., 105,* 437.
Robinson, K. W. and Lee, D. H. K. (1941): *Proc. roy. Soc. Queensland, 53,* 145.

STUDIES ON METABOLISM OF CREATINE AND CREATININE IN THE DOG

by

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It is generally known that in human beings creatine is normally excreted in urine of women in amounts fairly greater than in urine of men. Moreover, it was established that the excretion level is more or less raised during different phases of reproduction. The literature is lacking of data concerning the dog, and in a previous paper (Hehyawi, 1958) these data were obtained. The present investigation was undertaken to obtain data on creatine and creatinine excretion during normal phases of the reproductive cycle.

Experimental

Healthy female animals of various weights and ages were used in this study. Experimental details on normal diet, collection of urine, and determination of creatine and creatinine are similar to those described by Hehyawi (1958).

Results

The 24 hour urinary output of creatine and creatinine was determined frequently in 31 normal female animals. Table 1 illustrates the results obtained at different periods of the reproductive cycle, i.e. before and at puberty and during oestrous, pregnancy, labour, and puerperium.

Before puberty (3 to 4 months of age) the creatine excretion was much higher than its level at puberty. Contrary to creatine, creatinine excretion increased gradually as the animal approached puberty. The rise in creatinine observed in the second half of oestrus (last 3 or 4 days) was found to continue past oestrus in some normal bitches. Creatinine was also excreted in fairly high amounts.

A gradual rise in creatine excretion during pregnancy and a sudden additional rise of as much as about 5 mg. per cent. during labour are recorded in the Table. In few cases either or both of these increases might fail to occur.

In comparison with the non-pregnant state, no marked change was observed in creatinine excretion during pregnancy. The most consistent or significant change in urinary creatinine in normal pregnancy was found during the course of labour, when a striking drop in the rate of its excretion was encountered. Early in puerperium this

rise returned to normal non-pregnant level. Creatinuria appeared regularly during puerperium even in animals which did not show it at other times.

TABLE 1

Physiological changes in the excretion of creatine and creatinine in the urine of the normal bitch.

Number of Cases	Experimental Condition	Creatine		Creatinine	
		Mean	Range	Mean	Range
7	Before puberty	26.7	20.7-32.5	73	66-82
11	At puberty	18.3	0.0-21.3	121	116-128
8	Oestrus 1st half	16.8	13.2-21.7	135	130-140
8	Oestrus 2nd half	18.6	14.1-23.8	151	145-157
10	Pregnancy	39.3	35.0-49.1	132	127-136
8	Labour	43.6	40.7-54.0	80	71-92
6	Puerperium	28.5	24.6-34.4	129	122-138

Discussion

The increase in creatine excretion before puberty is evidently due to an increased production of creatine from its precursors during this time (Beard, 1943). The rise in creatinine output at puberty may be due to the increase in the muscular mass of the body at that time.

The definite change in creatine and creatinine metabolism during oestrus in the bitch may be attributed to change in water metabolism and vascularity accompanying oestrus rather than on the hormone secretion during that time (Smith, 1942). The high excretion value of creatine during labour may be due to increased muscular exertion during the course of this phase of the reproductive cycle. Again, the record by Harding, Allin, and Van Wyck (1924) on that the increase is more frequent in primiparae than in multiparae supports the failure in this study to find any increase in creatine level in some urinary samples during labour. These authors claim that the difference between the two conditions may be attributed to the greater muscular exertion of the primiparae during delivery.

During labour, the rise in the excretion of creatine and the corresponding fall in creatinine output confirms the findings by Harding and his co-workers that the presence of creatine in urine is usually associated with a compensatory reduction of the creatinine excretion.

Summary

The excretion of creatine and creatinine in 31 normal female dogs was studied under different phases of reproductive cycle.

1. At puberty the excretion of creatine was much reduced with respect to creatinuria before puberty.
2. A gradual rise was observed during normal pregnancy with a sudden additional rise during labour. There was no change in creatinine excretion throughout pregnancy with respect to the non-pregnant state.
3. During labour a striking fall in creatinine excretion was encountered.
4. Creatinuria was a constant finding in urine during puerperium.

REFERENCES

Beard, H. H. (1943): "Creatine and Creatinine Metabolism," 1st ed., Chemical Publishing Co., Brooklyn, N.Y., U.S.A.

Harding, V. J., Allin, K. D. and Van Wyck, H. B. (1924): *J. Obst. Gynaecol., 31,* 595.

Hehyawi, M. G. E. (1958): *Brit. Vet. J.* 114, 480.

Smith, O. W. (1942): *J. Clin. Endocrinol.,* **2,** 1.

REVIEW

HANDBUCH DER TIERZÜCHTUNG. Ed. John Hammond, Ivor Johansson and Fritz Haring. Band 1. Biologische Grundlage. ed. by John Hammand and Ivor Johansson. 1959. D.M. 98. Hamburg/Berlin. Paul Parey.

This is the first of three volumes which will appear under the general editorship of Dr. Hammond of the United Kingdom, Professor Johansson of Sweden and Professor Haring of Germany, and which are designed to provide a complete and authoritative text on animal breeding. Individual chapters will be contributed by specialists from all countries. The volume under review is edited by Hammond and Johansson and covers the general biological background necessary for the consideration of the problems of animal production and improvement. Whatever the nationality of the author all chapters appear in German, but in most cases in a style sufficiently simple to be understood by anyone with a nodding acquaintance with the language. In their choice of references several contributors indicate a certain insularity but this is a very minor defect in a work which deserves an enthusiastic reception. The volume includes chapters by Herre on the origin of the domestic animals, by Bane & Bonadonna on reproduction and its disorders, by Mitscherlich on artificial insemination, by Hammond on growth and meat production, by Witt on milk production, by Doehner on wool, by Mehner & Rauch on egg production, by Jull on the production of poultry for the table, by Phillips on ecology, by Kruger on performance testing in the various species and by Lörtschner on conformation. Most of these names will be familiar to British readers and will sufficiently vouch for the competence of the contributions, many of which well merit a separate review. Space does not permit an extensive survey of this work but if any chapter is to be singled out for special praise, let it be the first, by Herre, for the consideration of the origin of the domestic species and their relationship to their wild progenitors is a fascinating topic which has been neglected by the perhaps too practical British and American writers.

The publishers are to be congratulated upon this work which is beautifully produced. The cost may at first sight appear high but then this is really several books in one and it is worth every penny of its price.

VITAMINOTERAPIA EN CLÍNICA VETERINARIA (Vitamin Therapy in Clinical Veterinary Medicine) by J. D. Esteban Fernández and J. Séculi Brillas. Productos Neosan S.A., Barcelona. 1958. 370 pages.

This is a comprehensive review of the subject. Following an historical introduction each vitamin is dealt with separately. A general account is given of the vitamin, and the natural and experimental avitaminosis is described. Reference is made to the vitamin requirements of animals, and the therapeutic use of the vitamin is discussed. The accounts of avitaminosis are illustrated by photographs. A large number of references are quoted from all parts of the world. This monograph will be of interest to all those concerned with vitamins both in nutrition and in therapeutics.

OBITUARY

TOM HARE, M.D., C.H.B., B.V.Sc., M.R.C.V.S.

Dr. Tom Hare died at his home, 70 Holywell Hill, St. Albans, in the early morning of Tuesday, March 17th. He was the son and only child of George Hare, Chemist of Plumtree Square, Nottingham, and he was born on October 8th, 1895. He was educated at Loughborough Grammar School. He went to Liverpool University for the Autumn term of 1911. He had not taken his preliminary examination but he accomplished this task at the following Christmas, and he was formally enrolled as a veterinary student in 1912. One of his greatest friends has told me that right from the start Tom was a cut above the average student both in intelligence and address.

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His suits were always well made and of good style and he took great care of his personal appearance. He always checked up in front of the large mirror in the hall of their digs before going to the veterinary school. His academic career was interrupted by the first World War. He joined the Cheshire regiment and served throughout the war attaining the rank of Captain. After demobilisation he returned to the veterinary school and graduated M.R.C.V.S. on July 16th, 1921. He remained at the University and entered upon the medical course qualifying M.B., Ch.B. in 1924.

Tom did not give all his time to academic study. He was a good athlete, he played a good game as full back at Association Football, he was good on the tennis court and he was a first class "all rounder" at cricket. He played in the University First Eleven, became Captain of Cricket for the University, and he took an active part in student University affairs. He was President of the Guild of Undergraduates at Liverpool University and Chairman of the Inter-University Athletic Board of Great Britain and Ireland. After graduating in medicine he was appointed Thelwell Thomas Fellow in surgical pathology and later he held the Holt Fellowship in pathology at his University.

He was awarded the M.D. degree of his University in 1926. In March 1927 he was appointed Research Officer on Foot and Mouth disease by the Ministry of Agriculture and went to work at the Lister Institute, Chelsea. In September 1927 he succeeded Sir John MacFadyean as Professor of Pathology at the Royal Veterinary College. In 1933 he relinquished this post to become Director of the Veterinary Research Laboratories. Later he established his own pathological practice in Finchley Road which he conducted, in collaboration with A. B. Orr, B.Sc., M.R.C.V.S., until his death.

Tom Hare's main interest in life was centred in the veterinary profession. He took an active part in the counsels of the B.V.A. and of the Central and the Herts. and Beds. divisions of that association. He was a founder of the latter division and he served both divisions as President. He was an active member of the Society of Practising Veterinary Surgeons and served on the Council of that body. He served also for some years on the Council of the R.C.V.S. Although his first interest was in veterinary science Hare was active also in medical circles. He was a member of the B.M.A. and in 1938-39 he was Chairman of the St. Albans' Division. He was a member of the medical war committee of the Mid-Herts. Division throughout World War II. He was a Fellow and a Past President of the Harvein Society. His Presidential address was on "The Tudor Ancestry of Dr. William Harvey" and at the time of his death he was engaged in the writing of a book on Harvey.

Hare was a good and sincere Churchman and he took an active part in Church affairs. He was deeply interested in the Cathedral at St. Albans. He revelled in its architecture, its history and monuments and I understand he was gathering material in order to write a book on the subject. He was interested in archaeology and he was quite an authority on the remains of the Roman City of Verulam which it was his delight to show to friends. Antiques claimed his attention and no doubt his bent in this direction was inherited, for his father, a Fellow of the Thoroton Society, was one of the leading antiquarians in the Midlands. He was a keen student of the natural history of the countryside and especially of ornithology. He made many contributions to veterinary and medical literature on a great variety of subjects. His work on Arthritis, B-haemolytic streptococcal infections and parasitic infestation bore the mark of original thought and great technical skill and diligence. Many of his ideas and pronouncements were received at first with some scepticism by those who were shackled in the chains of orthodoxy. This did not daunt him and he lived to see his views accepted, in part if not in the whole, by those who had scoffed. He was an extremely competent morbid anatomist and in this he was held in high renown in medical and veterinary circles. He was not always a good advocate for his own cause in debate and he could irritate and annoy those who were of opposite opinion. He was not deterred by hostile opposition, indeed it served only to stir him to further effort and he would fight hard and persistently for any cause that his conscience told him to support. Those who were associated

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with him in any fight could depend on a loyal and constant ally who, come what may, would never let one down. Tom Hare was an "all round" pathologist, as were the masters of old, and he worked with equal facility in the realms of morbid anatomy, bacteriology, parasitology and protozoology. He was a good clinician also and before coming to a final conclusion he always tried to correlate the clinical history and signs with the pathological findings at the post-mortem examination. His reports, written invariably in his own hand, would give in great detail a complete pen picture of every facet of a case and often include valuable clinical therapeutic recommendations or suggestions.

Hare was a slim man of somewhat frail physique. His face was cast in a fine drawn mould and could register sorrow, anger or joy in a flash. All the time that I knew him he was never a fit man for he had been gassed in the first World War and was troubled in his chest. He walked with a stoop as if in contemplation. All his actions were marked with a delicate precision. He handled his microscope, specimens and the other tools of his trade as with a caress. The loading of his long cigarette holder was performed with great care and delicacy. When he was young he had such faith in his own views that he was wont to brush other opinions aside and in argument he could be awkward and obstructive, very awkward. He could be led but not driven. Those who knew him well excused his foibles for they knew that his thoughts and actions were directed by the heart and not by guile. As he grew older he mellowed considerably in address and he did not fly into action precipitously but, on occasion, the old fire would flash into flame if the rights and privileges of the veterinary profession were impinged to the slightest degree. A great "University" man and the holder of high degrees he, with his old teacher Share Jones, fought strenuously to try and preserve the old portal system of entry to the veterinary profession and the right of the profession to conduct and rule its own affairs. They lost, but they went down with colours flying and conscious of the gratitude and respect of the majority of the members of the profession. About a year ago his chest condition became worse and he was advised to submit himself to a serious operation. Many would have cringed from the prospect and especially so if they had possessed a tithe of Tom's knowledge of pathology. He bore his time of trial with great stoicism and bravery. At first it was thought that all might be well again but this was not to be. His knowledge of pathology must have told him of the course that events might run. He bore this with great composure, fortified and supported by his faith, for he had no fears of what was beyond the veil.

Tom was blessed in a happy marriage and family life. Mrs. Hare and he were good hosts and loved to entertain friends in their home. To Mrs. Hare and their children we extend our deepest sympathy and we hope that the knowledge that Tom Hare gained the respect and love of his peers will help them in their time of sorrow.

Tom Hare has left us the cherished memory of a kind, courteous and cultured gentleman who enriched his profession by his learning and strengthened it by his courageous actions.

NEWS

WELLCOME FOUNDATION'S DEVELOPMENT

On 1st May the first two completed stages of the five-year development plan of the Wellcome Research Laboratories, Beckenham, was declared open by Sir Henry Dale, O.M., F.R.S., Chairman of the Wellcome Trust.

The development programme, to provide up-to-date facilities for the Foundation's work in the field of research and the production of biological products, began in 1955. It is being carried through in three stages at a cost of over £2,000,000.

The Foundation has a long tradition of research achievement. Its founder, the late Sir Henry Wellcome, was a man of singular gifts and diverse interests. He was especially interested in research. The Wellcome Foundation pioneered in this field and has both a longer tradition of, and a larger stake in research than any similar organisation in the British Commonwealth.

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Beckenham is the Foundation's largest single research centre, but in addition the company's research activities are conducted also at the Wellcome Laboratories of Tropical Medicine in London; the Wellcome Veterinary Research Station at Frant; the Wellcome Research Laboratories at Tuckahoe, New York; and the Wellcome Research Laboratories (East Africa), Nairobi.

The Foundation's research work in the United Kingdom is organised into two main divisions, the Therapeutic Research Division and Biological Division. The work of the former is directed towards the discovery of new drugs.

The Biological Division, in addition to research covering a wide field of bacteriology, biochemistry, immunology and virology, is responsible for the development and large scale preparation of a comprehensive series of biological products for both human and veterinary use.

The first Wellcome biological product, Diphtheria Antitoxin, was issued in 1894, and since that time the laboratories have made outstanding contributions to medical and veterinary science. During the present century, the Company has pioneered in the biological field and is still the leading producer of biological products in the British Commonwealth. It is the largest producer of biological preparations for veterinary purposes in Europe and possibly in the world. For many years, the demand for Biological products has continued to increase, often outstripping production, particularly during the first and second World Wars when emergency measures to enhance protection had to be taken. In the period immediately following World War II the use of biological products was threatened by the rapid development of the new antibiotic drugs. The threat did not materialise, and the demand for new biological products increased and established products continued to be demanded in larger quantities than ever before. The range and number of individual products required for veterinary use also increased. To give one example, the laboratories today produce 13 seperate products for the diseases of sheep alone. In 1954, a position had been reached in which the available resources at Beckenham were so strained that research and development work was handicapped not only through lack of space, but because the advance in processing techniques made it necessary to provide increasingly higher standards of premises and plant. All these factors combined to emphasize the urgency of an extensive re-housing scheme, in which provision would be made for new and up-to-date laboratories.

Premises for the preparation of biological products demand the highest standards of cleanliness. In the case of virus vaccines, prepared from tissue culture, it is necessary to provide sterile working conditions no less exacting than those in the most modern surgical operating theatre. Research and development on virological products is a continuing activity, and necessitates a constant revision of methods and techniques. New premises must not only meet the strictest existing standards, but allow of conversion for new techniques of functions with the least disturbance to the work in hand, at the greatest possible speed and at the lowest possible cost.

All buildings designed for virological work need elaborate services, and before any planning of the buildings was considered, Wellcome architects, engineers and scientists inspected the most up-to-date laboratories in Europe and North America. They did not discover any existing design which appeared to embody all the requirements. Accordingly they set to work to evolve their own and this original and unique design was first incorporated in the building for the production of poliomyelitis vaccine. It proved to be so satisfactory that with certain modifications and improvements it was adopted as the proto-type for other buildings in the scheme.

In addition to the provision of the new buildings, extensive renovation of many of the older buildings at Beckenham has been, or is being, undertaken.

The new buildings for which provision has been made in Phases I, II, and III of the Beckenham development plan will provide some 180,000 sq. ft. of high grade laboratory accommodation at an average cost of approximately £10 per square foot. Renovations to older buildings will cost about £250,000 and when completed the five-year plan will have cost over £2,000,000.

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